



Clinical trial results:

TECOS: A Randomized, Placebo Controlled Clinical Trial to Evaluate Cardiovascular Outcomes after Treatment with Sitagliptin in Patients with Type 2 Diabetes Mellitus and Inadequate Glycemic Control

Summary

| | |
|--------------------------|--|
| EudraCT number | 2008-006719-20 |
| Trial protocol | LT NL DE ES HU LV FR CZ GB IE SK BG IT EE FI SE BE |
| Global end of trial date | 30 March 2015 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 |
| This version publication date | 09 April 2016 |
| First version publication date | 09 April 2016 |

Trial information

Trial identification

| | |
|-----------------------|-------------|
| Sponsor protocol code | MK-0431-082 |
|-----------------------|-------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00790205 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Merck Sharp & Dohme Corp. |
| Sponsor organisation address | 2000 Galloping Hill Road, Kenilworth, NJ, United States, 07033 |
| Public contact | Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com |
| Scientific contact | Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.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 | 30 March 2015 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 30 March 2015 |
| Global end of trial reached? | Yes |
| Global end of trial date | 30 March 2015 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

This is a clinical trial designed to assess the cardiovascular outcome of long-term treatment with sitagliptin used as part of usual care compared to usual care without sitagliptin in participants with Type 2 Diabetes Mellitus having a history of cardiovascular disease and a hemoglobin A1c (HbA1c) of 6.5% to 8.0%.

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice (GCP) standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

The following additional measure defined for this individual study was in place for the protection of trial subjects: in the event that a participant experiences severe hypoglycemia, usual care physicians will be notified and may adjust antihyperglycemic agent (AHA) medications in order to prevent or minimize the occurrence of further hypoglycemia.

Background therapy:

Background therapy included the following: stable doses of either monotherapy or dual combination therapy with metformin, pioglitazone, or a sulfonylurea, or, after a protocol amendment, stable doses of insulin (i.e., $\pm 20\%$ of the scheduled total daily insulin dose) either alone or in combination with metformin, for at least 3 months (i.e., no adjustments to oral antihyperglycemic therapy in the past 3 months).

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 10 December 2008 |
| 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: 542 |
| Country: Number of subjects enrolled | Australia: 427 |
| Country: Number of subjects enrolled | Belgium: 94 |
| Country: Number of subjects enrolled | Brazil: 406 |
| Country: Number of subjects enrolled | Bulgaria: 504 |
| Country: Number of subjects enrolled | Chile: 293 |
| Country: Number of subjects enrolled | China: 31 |
| Country: Number of subjects enrolled | Colombia: 230 |
| Country: Number of subjects enrolled | Canada: 549 |
| Country: Number of subjects enrolled | Czech Republic: 462 |
| Country: Number of subjects enrolled | Estonia: 88 |
| Country: Number of subjects enrolled | Finland: 50 |

| | |
|--------------------------------------|-------------------------|
| Country: Number of subjects enrolled | France: 86 |
| Country: Number of subjects enrolled | Germany: 503 |
| Country: Number of subjects enrolled | Hong Kong: 360 |
| Country: Number of subjects enrolled | Hungary: 565 |
| Country: Number of subjects enrolled | Israel: 362 |
| Country: Number of subjects enrolled | Italy: 192 |
| Country: Number of subjects enrolled | India: 1817 |
| Country: Number of subjects enrolled | Korea, Republic of: 330 |
| Country: Number of subjects enrolled | Latvia: 401 |
| Country: Number of subjects enrolled | Lithuania: 320 |
| Country: Number of subjects enrolled | Malaysia: 257 |
| Country: Number of subjects enrolled | Netherlands: 309 |
| Country: Number of subjects enrolled | Norway: 43 |
| Country: Number of subjects enrolled | New Zealand: 274 |
| Country: Number of subjects enrolled | Poland: 605 |
| Country: Number of subjects enrolled | Romania: 345 |
| Country: Number of subjects enrolled | Russian Federation: 465 |
| Country: Number of subjects enrolled | Singapore: 91 |
| Country: Number of subjects enrolled | Slovakia: 110 |
| Country: Number of subjects enrolled | South Africa: 406 |
| Country: Number of subjects enrolled | Spain: 202 |
| Country: Number of subjects enrolled | Sweden: 81 |
| Country: Number of subjects enrolled | Taiwan: 210 |
| Country: Number of subjects enrolled | Turkey: 100 |
| Country: Number of subjects enrolled | United Kingdom: 516 |
| Country: Number of subjects enrolled | United States: 2045 |
| Worldwide total number of subjects | 14671 |
| EEA total number of subjects | 5476 |

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) | 6764 |
| From 65 to 84 years | 7804 |
| 85 years and over | 103 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 14,671 participants were randomized to treatment, provided consent and did not have any GCP deviations.

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 |

Arms

| | |
|------------------------------|-------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Sitagliptin |

Arm description:

Sitagliptin tablet taken orally once daily in the morning

| | |
|--|-----------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Sitagliptin phosphate |
| Investigational medicinal product code | MK-0431 |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Sitagliptin phosphate, one 50 mg or 100 mg tablet (dose dependant on renal function) orally, once daily

| | |
|------------------|---------|
| Arm title | Placebo |
|------------------|---------|

Arm description:

Matching placebo tablet taken orally once daily in the morning

| | |
|--|----------|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Placebo tablet matching the 50 mg or 100 mg sitagliptin phosphate tablet orally, once daily

| Number of subjects in period 1 | Sitagliptin | Placebo |
|---------------------------------------|-------------|---------|
| Started | 7332 | 7339 |
| Treated | 7266 | 7274 |
| Completed | 6972 | 6905 |
| Not completed | 360 | 434 |

| | | |
|------------------------------|-----|-----|
| Consent withdrawn by subject | 299 | 363 |
| Lost to follow-up | 61 | 71 |

Baseline characteristics

Reporting groups

| | |
|--|-------------|
| Reporting group title | Sitagliptin |
| Reporting group description: | |
| Sitagliptin tablet taken orally once daily in the morning | |
| Reporting group title | Placebo |
| Reporting group description: | |
| Matching placebo tablet taken orally once daily in the morning | |

| Reporting group values | Sitagliptin | Placebo | Total |
|--|-------------|---------|-------|
| Number of subjects | 7332 | 7339 | 14671 |
| Age categorical | | | |
| Age was unavailable due to regulatory restrictions for 320 participants. The distribution of age in the other study participants was used to impute ages for those 320 participants in the "Age group breakdown for Trial" under the "Population of Trial Subjects" section of the record. | | | |
| Units: Subjects | | | |
| Adults (18-64 years) | 3315 | 3301 | 6616 |
| From 65-84 years | 3813 | 3821 | 7634 |
| 85 years and over | 46 | 55 | 101 |
| Unknown age | 158 | 162 | 320 |
| Gender, Male/Female | | | |
| Units: Participants | | | |
| Female | 2134 | 2163 | 4297 |
| Male | 5198 | 5176 | 10374 |
| Estimated glomerular filtration rate (eGFR) | | | |
| Sitagliptin, n=7254; Placebo, n=7274 | | | |
| Units: mL/min/1.73 m ² | | | |
| arithmetic mean | 74.9 | 74.9 | |
| standard deviation | ± 21.3 | ± 20.9 | - |
| Hemoglobin A1c (HbA1c) | | | |
| Sitagliptin, n=7330; Placebo, n=7336 | | | |
| Units: Percentage of HbA1c | | | |
| arithmetic mean | 7.2 | 7.2 | |
| standard deviation | ± 0.5 | ± 0.5 | - |
| Urine albumin:creatinine ratio | | | |
| Sitagliptin, n=2606; Placebo, n=2542 | | | |
| Units: g/mol Creatinine | | | |
| arithmetic mean | 8.6 | 8.4 | |
| standard deviation | ± 37.4 | ± 36 | - |

End points

End points reporting groups

| | |
|--|-------------|
| Reporting group title | Sitagliptin |
| Reporting group description: Sitagliptin tablet taken orally once daily in the morning | |
| Reporting group title | Placebo |
| Reporting group description: Matching placebo tablet taken orally once daily in the morning | |

Primary: Percentage of participants with first confirmed cardiovascular (CV) event of Major Adverse Cardiovascular Event (MACE) plus (Per protocol population)

| | |
|---|---|
| End point title | Percentage of participants with first confirmed cardiovascular (CV) event of Major Adverse Cardiovascular Event (MACE) plus (Per protocol population) |
| End point description: Primary composite CV endpoint of MACE plus which includes CV-related death, nonfatal myocardial infarction (MI), nonfatal stroke, or unstable angina requiring hospitalization. Per protocol population included all randomized participants who received study medication except those participants who did not contribute at least 1 day of data to the study analysis due to a major protocol violation that excluded all of their data. | |
| End point type | Primary |
| End point timeframe: Up to 5 years | |

| End point values | Sitagliptin | Placebo | | |
|-----------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 7257 | 7266 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 9.6 | 9.6 | | |

Statistical analyses

| | |
|---|------------------------------|
| Statistical analysis title | Between-treatment difference |
| Statistical analysis description: Hazard Ratio (HR) of Sitagliptin/Placebo: the between-treatment difference in time to the first primary composite CV endpoint was assessed by the HR between the sitagliptin and placebo groups. The confidence interval for the HR was computed and compared to 1.30, the non-inferiority margin. | |
| Comparison groups | Sitagliptin v Placebo |

| | |
|---|--------------------------------|
| Number of subjects included in analysis | 14523 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | < 0.001 ^[1] |
| Method | Cox proportional hazards model |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.98 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.88 |
| upper limit | 1.09 |

Notes:

[1] - Model stratified by region with treatment group only as explanatory variable.

Primary: Percentage of participants with first confirmed CV event of MACE plus (Intent to treat population)

| | |
|---|--|
| End point title | Percentage of participants with first confirmed CV event of MACE plus (Intent to treat population) |
| End point description: | |
| Primary composite CV endpoint of MACE plus which includes CV-related death, nonfatal MI, nonfatal stroke, or unstable angina requiring hospitalization. Intent to treat population included all randomized participants who received study medication, provided consent, and did not have any GCP deviations. | |
| End point type | Primary |
| End point timeframe: | |
| Up to 5 years | |

| End point values | Sitagliptin | Placebo | | |
|-----------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 7332 | 7339 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 11.4 | 11.6 | | |

Statistical analyses

| | |
|---|------------------------------|
| Statistical analysis title | Between-treatment difference |
| Statistical analysis description: | |
| HR of Sitagliptin/Placebo: the between-treatment difference in time to the first primary composite CV endpoint was assessed by the HR between the sitagliptin and placebo groups. The confidence interval for the HR was computed and compared to 1.30, the non-inferiority margin. | |
| Comparison groups | Sitagliptin v Placebo |

| | |
|---|--------------------------------|
| Number of subjects included in analysis | 14671 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | < 0.001 ^[2] |
| Method | Cox proportional hazards model |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.98 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.89 |
| upper limit | 1.08 |

Notes:

[2] - Model stratified by region with treatment group as the only explanatory variable.

Secondary: Percentage of participants with first confirmed CV event of MACE (Per protocol population)

| | |
|-----------------|--|
| End point title | Percentage of participants with first confirmed CV event of MACE (Per protocol population) |
|-----------------|--|

End point description:

CV composite endpoint of MACE which includes CV-related death, nonfatal MI, or nonfatal stroke. Per protocol population included all randomized participants who received study medication except those participants who did not contribute at least 1 day of data to the study analysis due to a major protocol violation that excluded all of their data.

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

End point timeframe:

Up to 5 years

| End point values | Sitagliptin | Placebo | | |
|-----------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 7257 | 7266 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 8.4 | 8.3 | | |

Statistical analyses

| | |
|----------------------------|------------------------------|
| Statistical analysis title | Between-treatment difference |
|----------------------------|------------------------------|

Statistical analysis description:

HR of Sitagliptin/Placebo: the between-treatment difference in time to the first primary composite CV endpoint was assessed by the HR between the sitagliptin and placebo groups. The confidence interval for the HR was computed and compared to 1.30, the non-inferiority margin.

| | |
|-------------------|-----------------------|
| Comparison groups | Sitagliptin v Placebo |
|-------------------|-----------------------|

| | |
|---|--------------------------------|
| Number of subjects included in analysis | 14523 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | < 0.001 ^[3] |
| Method | Cox proportional hazards model |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.99 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.89 |
| upper limit | 1.11 |

Notes:

[3] - Model stratified by region with treatment group only as explanatory variable.

Secondary: Percentage of participants with first confirmed CV event of MACE (Intent to treat population)

| | |
|-----------------|---|
| End point title | Percentage of participants with first confirmed CV event of MACE (Intent to treat population) |
|-----------------|---|

End point description:

CV composite endpoint of MACE which includes CV-related death, nonfatal MI, or nonfatal stroke. Intent to treat population included all randomized participants who received study medication, provided consent, and did not have any GCP deviations.

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

End point timeframe:

Up to 5 years

| End point values | Sitagliptin | Placebo | | |
|-----------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 7332 | 7339 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 10.2 | 10.2 | | |

Statistical analyses

| | |
|----------------------------|------------------------------|
| Statistical analysis title | Between-treatment difference |
|----------------------------|------------------------------|

Statistical analysis description:

HR of Sitagliptin/Placebo: the between-treatment difference in time to the first primary composite CV endpoint was assessed by the HR between the sitagliptin and placebo groups. The confidence interval for the HR was computed and compared to 1.30, the non-inferiority margin.

| | |
|-------------------|-----------------------|
| Comparison groups | Sitagliptin v Placebo |
|-------------------|-----------------------|

| | |
|---|--------------------------------|
| Number of subjects included in analysis | 14671 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | < 0.001 ^[4] |
| Method | Cox proportional hazards model |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.99 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.89 |
| upper limit | 1.1 |

Notes:

[4] - Model stratified by region with treatment group only as explanatory variable.

Secondary: Percent incidence of all cause mortality (Per protocol population)

| | |
|-----------------|--|
| End point title | Percent incidence of all cause mortality (Per protocol population) |
|-----------------|--|

End point description:

Percent incidence of all cause mortality is reported as the percentage of participants who died due to any cause. Per protocol population included all randomized participants who received study medication except those participants who did not contribute at least 1 day of data to the study analysis due to a major protocol violation that excluded all of their data.

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

End point timeframe:

Up to 5 years

| End point values | Sitagliptin | Placebo | | |
|-----------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 7257 | 7266 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 4.7 | 4.3 | | |

Statistical analyses

| | |
|----------------------------|------------------------------|
| Statistical analysis title | Between-treatment difference |
|----------------------------|------------------------------|

Statistical analysis description:

HR of Sitagliptin/Placebo: the between-treatment difference in mortality due to all causes was assessed by the HR between the sitagliptin and placebo groups.

| | |
|---|--------------------------------|
| Comparison groups | Sitagliptin v Placebo |
| Number of subjects included in analysis | 14523 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.435 |
| Method | Cox proportional hazards model |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.06 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.91 |
| upper limit | 1.24 |

Secondary: Percent incidence of all cause mortality (Intent to treat population)

| | |
|---|---|
| End point title | Percent incidence of all cause mortality (Intent to treat population) |
| End point description: | |
| Percent incidence of all cause mortality is reported as the percentage of participants who died due to any cause. Intent to treat population included all randomized participants who received study medication, provided consent, and did not have any GCP deviations. | |
| End point type | Secondary |
| End point timeframe: | |
| Up to 5 years | |

| End point values | Sitagliptin | Placebo | | |
|-----------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 7332 | 7339 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 7.5 | 7.3 | | |

Statistical analyses

| | |
|---|--------------------------------|
| Statistical analysis title | Between-treatment difference |
| Statistical analysis description: | |
| HR of Sitagliptin/Placebo: the between-treatment difference in mortality due to all causes was assessed by the HR between the sitagliptin and placebo groups. | |
| Comparison groups | Sitagliptin v Placebo |
| Number of subjects included in analysis | 14671 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.875 |
| Method | Cox proportional hazards model |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.01 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.9 |
| upper limit | 1.14 |

Secondary: Percent incidence of congestive heart failure requiring hospitalization (Per protocol population)

| | |
|-----------------|---|
| End point title | Percent incidence of congestive heart failure requiring hospitalization (Per protocol population) |
|-----------------|---|

End point description:

Percent incidence of congestive heart failure requiring hospitalization is reported as the percentage of participants who were admitted to the hospital for congestive heart failure. Per protocol population included all randomized participants who received study medication except those participants who did not contribute at least 1 day of data to the study analysis due to a major protocol violation that excluded all of their data.

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

End point timeframe:

Up to 5 years

| End point values | Sitagliptin | Placebo | | |
|-----------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 7257 | 7266 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 2.8 | 2.8 | | |

Statistical analyses

| | |
|----------------------------|------------------------------|
| Statistical analysis title | Between-treatment difference |
|----------------------------|------------------------------|

Statistical analysis description:

Hazard Ratio of Sitagliptin/Placebo: The between-treatment difference in congestive heart failure cases requiring hospitalization was assessed by the hazard ratio between the Sitagliptin and Placebo groups.

| | |
|---|--------------------------------|
| Comparison groups | Sitagliptin v Placebo |
| Number of subjects included in analysis | 14523 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.858 ^[5] |
| Method | Cox proportional hazards model |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.98 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.81 |
| upper limit | 1.19 |

Notes:

[5] - Model stratified by region with treatment group and history of congestive heart failure at baseline as explanatory variables.

Secondary: Percent incidence of congestive heart failure requiring hospitalization (Intent to treat population)

| | |
|---|--|
| End point title | Percent incidence of congestive heart failure requiring hospitalization (Intent to treat population) |
| End point description: Percent incidence of congestive heart failure requiring hospitalization is reported as the percentage of participants who were admitted to the hospital for congestive heart failure. Intent to treat population included all randomized participants who received study medication, provided consent, and did not have any GCP deviations. | |
| End point type | Secondary |
| End point timeframe: Up to 5 years | |

| End point values | Sitagliptin | Placebo | | |
|-----------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 7332 | 7339 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 3.1 | 3.1 | | |

Statistical analyses

| | |
|---|--------------------------------|
| Statistical analysis title | Between-treatment difference |
| Statistical analysis description: Hazard Ratio of Sitagliptin/Placebo: The between-treatment difference in congestive heart failure cases requiring hospitalization was assessed by the hazard ratio between the Sitagliptin and Placebo groups. | |
| Comparison groups | Sitagliptin v Placebo |
| Number of subjects included in analysis | 14671 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.983 [6] |
| Method | Cox proportional hazards model |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.83 |
| upper limit | 1.2 |

Notes:

[6] - Model stratified by region with treatment group and history of congestive heart failure at baseline as explanatory variable.

Secondary: Change from baseline in renal function over time (Per protocol population)

| | |
|-----------------|--|
| End point title | Change from baseline in renal function over time (Per protocol population) |
|-----------------|--|

End point description:

Change in renal function based on estimated glomerular filtration rate [eGFR] using the Modification of Diet in Renal Disease [MDRD] method. Per protocol population included all randomized participants who received study medication except those participants who did not contribute at least 1 day of data to the study analysis due to a major protocol violation that excluded all of their data.

| | |
|----------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline and up to 5 years | |

| End point values | Sitagliptin | Placebo | | |
|--|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 7257 | 7266 | | |
| Units: mL/min/1.73 m ² | | | | |
| arithmetic mean (standard deviation) | | | | |
| Month 4; Sitagliptin, n=3859, Placebo, n=3864 | -1.9 (± 14.2) | -0.8 (± 14.3) | | |
| Month 8; Sitagliptin, n=3562, Placebo, n=3501 | -2.5 (± 14.9) | -0.9 (± 15.1) | | |
| Month 12; Sitagliptin, n=4912, Placebo, n=4778 | -1.8 (± 15.8) | -0.5 (± 16.2) | | |
| Month 24; Sitagliptin, n=4782, Placebo, n=4636 | -3.1 (± 17.9) | -1.7 (± 17.5) | | |
| Month 36; Sitagliptin, n=2776, Placebo, n=2614 | -3.7 (± 18) | -1.6 (± 18.8) | | |
| Month 48; Sitagliptin, n=1096, Placebo, n=1056 | -3.7 (± 18.3) | -2.8 (± 18.4) | | |
| Month 60; Sitagliptin, n=79, Placebo, n=88 | -3.5 (± 18.2) | -6.4 (± 17.3) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in renal function over time (Intent to treat population)

| | |
|--|---|
| End point title | Change from baseline in renal function over time (Intent to treat population) |
| End point description: | |
| Change in renal function based on estimated glomerular filtration rate [eGFR] using the Modification of Diet in Renal Disease [MDRD] method. Intent to treat population included all randomized participants who received study medication, provided consent, and did not have any GCP deviations. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline and up to 5 years | |

| End point values | Sitagliptin | Placebo | | |
|---|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 7332 | 7339 | | |
| Units: mL/min/ 1.73 m ² | | | | |
| arithmetic mean (standard deviation) | | | | |
| Month 4; Sitagliptin, n=3949, Placebo, n=3977 | -1.8 (± 14.3) | -0.8 (± 14.3) | | |

| | | | | |
|--|---------------|---------------|--|--|
| Month 8; Sitagliptin, n=3687; Placebo, n=3648 | -2.4 (± 14.8) | -0.9 (± 15.2) | | |
| Month 12; Sitagliptin, n=5082, Placebo, n=5015 | -1.8 (± 15.8) | -0.5 (± 16.3) | | |
| Month 24; Sitagliptin, n=5157, Placebo, n=5071 | -3.2 (± 17.9) | -1.7 (± 17.7) | | |
| Month 36; Sitagliptin, n=3037, Placebo, n=2942 | -3.8 (± 18.1) | -1.6 (± 18.7) | | |
| Month 48; Sitagliptin, n=1237, Placebo, n=1210 | -4 (± 18.4) | -2.8 (± 18.3) | | |
| Month 60; Sitagliptin, n=93, Placebo, n=106 | -4.2 (± 17.4) | -5.7 (± 17.2) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in HbA1c over time (Per protocol population)

| | |
|-----------------|---|
| End point title | Change from baseline in HbA1c over time (Per protocol population) |
|-----------------|---|

End point description:

HbA1c is a measure of the percentage of glycated hemoglobin in the blood. Estimated mean difference between sitagliptin and placebo controlling for baseline HbA1c and region. Per protocol population included all randomized participants who received study medication except those participants who did not contribute at least 1 day of data to the study analysis due to a major protocol violation that excluded all of their data.

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

End point timeframe:

Baseline and up to 4 years

| End point values | Sitagliptin | Placebo | | |
|--|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 7257 | 7266 | | |
| Units: Percentage of HbA1c | | | | |
| arithmetic mean (standard deviation) | | | | |
| Month 4; Sitagliptin, n=6632, Placebo, n=6588 | -0.3 (± 0.8) | 0.1 (± 0.9) | | |
| Month 8; Sitagliptin, n=6294, Placebo, n=6197 | -0.3 (± 0.9) | 0.1 (± 1) | | |
| Month 12; Sitagliptin, n=6217, Placebo, n=6092 | -0.2 (± 1) | 0.1 (± 1) | | |
| Month 24; Sitagliptin, n=5668, Placebo, n=5475 | -0.1 (± 1) | 0.2 (± 1.1) | | |
| Month 36; Sitagliptin, n=3227, Placebo, n=3083 | -0.1 (± 1.1) | 0.1 (± 1.1) | | |
| Month 48; Sitagliptin, n=1271, Placebo, n=1224 | 0 (± 1.1) | 0.1 (± 1.2) | | |
| Month 60; Sitagliptin, n=106, Placebo, n=108 | -0.1 (± 1) | 0 (± 0.9) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in HbA1c over time (Intent to treat population)

| | |
|--|--|
| End point title | Change from baseline in HbA1c over time (Intent to treat population) |
| End point description: HbA1c is a measure of the percentage of glycated hemoglobin in the blood. Estimated mean difference between sitagliptin and placebo controlling for baseline HbA1c and region. Intent to treat population included all randomized participants who received study medication, provided consent, and did not have any GCP deviations. | |
| End point type | Secondary |
| End point timeframe: Baseline and up to 4 years | |

| End point values | Sitagliptin | Placebo | | |
|--|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 7332 | 7339 | | |
| Units: Percentage of HbA1c | | | | |
| arithmetic mean (standard deviation) | | | | |
| Month 4; Sitagliptin, n=6772, Placebo, n=6738 | -0.3 (± 0.8) | 0.1 (± 0.9) | | |
| Month 8; Sitagliptin, n=6478; Placebo, n=6414 | -0.2 (± 0.9) | 0.1 (± 1) | | |
| Month 12; Sitagliptin, n=6448; Placebo, n=6384 | -0.2 (± 1) | 0.1 (± 1) | | |
| Month 24; Sitagliptin, n=6105; Placebo, n=5975 | -0.1 (± 1) | 0.1 (± 1.1) | | |
| Month 36; Sitagliptin, n=3521; Placebo, n=3439 | -0.1 (± 1.1) | 0.1 (± 1.1) | | |
| Month 48; Sitagliptin, n=1432; Placebo, n=1383 | 0 (± 1.1) | 0.1 (± 1.2) | | |
| Month 60; Sitagliptin, n=123; Placebo, n=128 | 0 (± 1) | 0 (± 1) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in urine albumin:creatinine ratio over time (Per protocol population)

| | |
|-----------------|---|
| End point title | Change from baseline in urine albumin:creatinine ratio over |
|-----------------|---|

| | |
|---|--------------------------------|
| | time (Per protocol population) |
| End point description: | |
| Change from baseline reflects the difference between the urine albumin:creatinine ratio reported time point and baseline value. Per protocol population included all randomized participants who received study medication except those participants who did not contribute at least 1 day of data to the study analysis due to a major protocol violation that excluded all of their data. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline and up to 5 years | |

| End point values | Sitagliptin | Placebo | | |
|--|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 7257 | 7266 | | |
| Units: g/mol Creatinine | | | | |
| arithmetic mean (standard deviation) | | | | |
| Month 4; Sitagliptin, n=664, Placebo, n=688 | -2.2 (± 27.7) | -1.4 (± 24.6) | | |
| Month 8; Sitagliptin, n=635, Placebo, n=597 | 1.7 (± 38.5) | 0.2 (± 45.3) | | |
| Month 12; Sitagliptin, n=1126, Placebo, n=1059 | 0.8 (± 27.7) | 1.2 (± 33.1) | | |
| Month 24; Sitagliptin, n=930, Placebo, n=892 | 0.7 (± 34) | 3.2 (± 31.6) | | |
| Month 36; Sitagliptin, n=488, Placebo, n=513 | 2.5 (± 24) | 4 (± 31) | | |
| Month 48; Sitagliptin, n=238, Placebo, n=233 | 1.3 (± 15.2) | 1.5 (± 25.5) | | |
| Month 60; Sitagliptin, n=13, Placebo, n=17 | -2.7 (± 10.1) | 4.8 (± 15.4) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in urine albumin:creatinine ratio over time (Intent to treat population)

| | |
|---|---|
| End point title | Change from baseline in urine albumin:creatinine ratio over time (Intent to treat population) |
| End point description: | |
| Change from baseline reflects the difference between the urine albumin:creatinine ratio reported time point and baseline value. Intent to treat population included all randomized participants who received study medication, provided consent, and did not have any GCP deviations. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline and up to 5 years | |

| End point values | Sitagliptin | Placebo | | |
|--|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 7332 | 7339 | | |
| Units: g/mol Creatinine | | | | |
| arithmetic mean (standard deviation) | | | | |
| Month 4; Sitagliptin, n=677, Placebo, n=713 | -2.1 (± 27.5) | -1.4 (± 24.1) | | |
| Month 8; Sitagliptin, n=658, Placebo, n=624 | 2.1 (± 39.4) | 0.5 (± 44.5) | | |
| Month 12; Sitagliptin, n=1167, Placebo, n=1115 | 1.3 (± 30.2) | 1.2 (± 32.3) | | |
| Month 24; Sitagliptin, n=1011, Placebo, n=964 | 0.5 (± 33.1) | 3.1 (± 30.7) | | |
| Month 36; Sitagliptin, n=537, Placebo, n=553 | 2.6 (± 25.8) | 3.9 (± 30.3) | | |
| Month 48; Sitagliptin, n=265, Placebo, n=256 | 1.9 (± 16.3) | 1.6 (± 24.5) | | |
| Month 60; Sitagliptin, n=14, Placebo, n=18 | -2.5 (± 9.7) | 6.4 (± 16.4) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants who initiated chronic insulin therapy (Per protocol population)

| | |
|-----------------|--|
| End point title | Percentage of participants who initiated chronic insulin therapy (Per protocol population) |
|-----------------|--|

End point description:

Chronic insulin therapy is defined as a continuous period of insulin use of more than 3 months. Per protocol population included all randomized participants who received study medication except those participants who did not contribute at least 1 day of data to the study analysis due to a major protocol violation that excluded all of their data.

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

End point timeframe:

Up to 5 years

| End point values | Sitagliptin | Placebo | | |
|-----------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 5554 | 5601 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 8.6 | 11.9 | | |

Statistical analyses

| | |
|---|-------------------------------|
| Statistical analysis title | Between-treatment difference |
| Comparison groups | Sitagliptin v Placebo |
| Number of subjects included in analysis | 11155 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.001 ^[7] |
| Method | Cox propotional hazards model |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.69 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.61 |
| upper limit | 0.77 |

Notes:

[7] - Model stratified by region with treatment group only as explanatory variable.

Secondary: Percentage of participants who initiated chronic insulin therapy (Intent to treat population)

| | |
|------------------------|---|
| End point title | Percentage of participants who initiated chronic insulin therapy (Intent to treat population) |
| End point description: | Chronic insulin therapy is defined as a continuous period of insulin use of more than 3 months. Intent to treat population included all randomized participants who received study medication, provided consent, and did not have any GCP deviations. |
| End point type | Secondary |
| End point timeframe: | |
| Up to 5 years | |

| End point values | Sitagliptin | Placebo | | |
|-----------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 5608 | 5655 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 9.7 | 13.2 | | |

Statistical analyses

| | |
|---|--------------------------------|
| Statistical analysis title | Between-treatment difference |
| Comparison groups | Sitagliptin v Placebo |
| Number of subjects included in analysis | 11263 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.001 ^[8] |
| Method | Cox proportional hazards model |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.7 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.63 |
| upper limit | 0.79 |

Notes:

[8] - Model stratified by region with treatment group as only explanatory variable.

Secondary: Percentage of participants who initiated a co-interventional agent (Per protocol population)

| | |
|-----------------|--|
| End point title | Percentage of participants who initiated a co-interventional agent (Per protocol population) |
|-----------------|--|

End point description:

In participants not receiving insulin at baseline, addition of first co-interventional agent was the addition of next oral antihyperglycemic agent (AHA) or chronic insulin, where chronic insulin therapy is defined as a continuous period of insulin use of more than 3 months. Per protocol population included all randomized participants who received study medication except those participants who did not contribute at least 1 day of data to the study analysis due to a major protocol violation that excluded all of their data.

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

End point timeframe:

Up to 5 years

| End point values | Sitagliptin | Placebo | | |
|-----------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 7257 | 7266 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 18.9 | 24.5 | | |

Statistical analyses

| | |
|---|--------------------------------|
| Statistical analysis title | Between-treatment difference |
| Comparison groups | Sitagliptin v Placebo |
| Number of subjects included in analysis | 14523 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.001 [9] |
| Method | Cox proportional hazards model |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.7 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.65 |
| upper limit | 0.75 |

Notes:

[9] - Model stratified by region with treatment group only as explanatory variable.

Secondary: Percentage of participants who initiated a co-interventional agent (Intent to treat population)

| | |
|-----------------|---|
| End point title | Percentage of participants who initiated a co-interventional agent (Intent to treat population) |
|-----------------|---|

End point description:

In participants not receiving insulin at baseline, addition of first co-interventional agent was the addition of next oral antihyperglycemic agent (AHA) or chronic insulin, where chronic insulin therapy is defined as a continuous period of insulin use of more than 3 months. Intent to treat population included all randomized participants who received study medication, provided consent, and did not have any GCP deviations.

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

End point timeframe:

Up to 5 years

| End point values | Sitagliptin | Placebo | | |
|-----------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 7332 | 7339 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 21.7 | 27.9 | | |

Statistical analyses

| | |
|---|---------------------------------------|
| Statistical analysis title | Between-treatment difference |
| Comparison groups | Sitagliptin v Placebo |
| Number of subjects included in analysis | 14671 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | < 0.001 ^[10] |
| Method | Method Cox proportional hazards model |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.72 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.68 |
| upper limit | 0.77 |

Notes:

[10] - Model stratified by region with treatment group only as explanatory variable.

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

Up to 68 months (including up to 28 days after last dose of study drug)

Adverse event reporting additional description:

All participants as treated (APaT) population includes participants who received at least one dose of study drug.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 17.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description:

Matching placebo tablet taken orally once daily in the morning

| | |
|-----------------------|-------------|
| Reporting group title | Sitagliptin |
|-----------------------|-------------|

Reporting group description:

Sitagliptin tablet taken orally once daily in the morning

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: No non-serious adverse events exceeded the 5% threshold for any treatment group.

| Serious adverse events | Placebo | Sitagliptin | |
|---|------------------------|------------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 909 / 7274 (12.50%) | 928 / 7266 (12.77%) | |
| number of deaths (all causes) | 57 | 54 | |
| number of deaths resulting from adverse events | 3 | 0 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Abdominal neoplasm | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Acute myeloid leukaemia | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Adenocarcinoma | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|-------------------|-------------------|--|
| Adenocarcinoma gastric | | | |
| subjects affected / exposed | 2 / 7274 (0.03%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Adenocarcinoma of appendix | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Adenocarcinoma of colon | | | |
| subjects affected / exposed | 12 / 7274 (0.16%) | 11 / 7266 (0.15%) | |
| occurrences causally related to treatment / all | 1 / 12 | 0 / 11 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Adenocarcinoma of salivary gland | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Adenocarcinoma of the cervix | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Adenocarcinoma pancreas | | | |
| subjects affected / exposed | 2 / 7274 (0.03%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 1 / 1 | 0 / 2 | |
| Adenoid cystic carcinoma | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Adenolymphoma | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anal cancer | | | |

| | | | |
|---|-------------------|-------------------|--|
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anal squamous cell carcinoma | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anaplastic large-cell lymphoma | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Angioimmunoblastic T-cell lymphoma | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (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 | 4 / 7274 (0.05%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Basal cell carcinoma | | | |
| subjects affected / exposed | 55 / 7274 (0.76%) | 44 / 7266 (0.61%) | |
| occurrences causally related to treatment / all | 0 / 86 | 0 / 50 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Basosquamous carcinoma | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Benign gastric neoplasm | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Benign salivary gland neoplasm | | | |

| | | | |
|---|-------------------|-------------------|--|
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bile duct cancer | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 3 / 7266 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 2 | |
| Bladder cancer | | | |
| subjects affected / exposed | 10 / 7274 (0.14%) | 15 / 7266 (0.21%) | |
| occurrences causally related to treatment / all | 0 / 10 | 0 / 15 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 2 | |
| Bladder cancer recurrent | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| 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 | 2 / 7274 (0.03%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bladder papilloma | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bladder transitional cell carcinoma | | | |
| subjects affected / exposed | 6 / 7274 (0.08%) | 6 / 7266 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 6 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Bone cancer | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bone neoplasm | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bone sarcoma | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bowen's disease | | | |
| subjects affected / exposed | 2 / 7274 (0.03%) | 4 / 7266 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 2 | 1 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Breast cancer | | | |
| subjects affected / exposed | 5 / 7274 (0.07%) | 5 / 7266 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Breast cancer in situ | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Breast cancer metastatic | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Breast cancer recurrent | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchial carcinoma | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 3 / 7266 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 2 | |
| Carcinoid tumour of the small bowel | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Carcinoid tumour pulmonary | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Central nervous system lymphoma | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Cervix carcinoma | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholangiocarcinoma | | | |
| subjects affected / exposed | 4 / 7274 (0.05%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 2 | 0 / 1 | |
| Cholesteatoma | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chronic lymphocytic leukaemia | | | |
| subjects affected / exposed | 3 / 7274 (0.04%) | 4 / 7266 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Chronic lymphocytic leukaemia recurrent | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chronic myeloid leukaemia | | | |

| | | | |
|---|-------------------|-------------------|--|
| subjects affected / exposed | 3 / 7274 (0.04%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Clear cell renal cell carcinoma | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Colon adenoma | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 4 / 7266 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colon cancer | | | |
| subjects affected / exposed | 14 / 7274 (0.19%) | 11 / 7266 (0.15%) | |
| occurrences causally related to treatment / all | 0 / 14 | 0 / 11 | |
| deaths causally related to treatment / all | 0 / 4 | 0 / 0 | |
| Colon cancer metastatic | | | |
| subjects affected / exposed | 2 / 7274 (0.03%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colon cancer stage I | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| 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 | 2 / 7274 (0.03%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colon neoplasm | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colorectal adenocarcinoma | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 2 / 7274 (0.03%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Colorectal cancer | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diffuse large B-cell lymphoma | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Endometrial adenocarcinoma | | | |
| subjects affected / exposed | 5 / 7274 (0.07%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Endometrial cancer | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gallbladder cancer | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastric adenoma | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| 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 | 2 / 7274 (0.03%) | 5 / 7266 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Gastric cancer recurrent | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 7274 (0.01%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Gastric cancer stage IV | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal cancer metastatic | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal carcinoma | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal tract adenoma | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Glioblastoma multiforme | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Glioma | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatic cancer | | | |
| subjects affected / exposed | 2 / 7274 (0.03%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 2 | 0 / 0 | |
| Hepatic cancer metastatic | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 7274 (0.00%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Hepatic neoplasm | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatocellular carcinoma | | | |
| subjects affected / exposed | 3 / 7274 (0.04%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 3 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Intraductal papilloma of breast | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intraductal proliferative breast lesion | | | |
| subjects affected / exposed | 2 / 7274 (0.03%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intraocular melanoma | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Invasive ductal breast carcinoma | | | |
| subjects affected / exposed | 4 / 7274 (0.05%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 1 / 4 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Laryngeal cancer | | | |
| subjects affected / exposed | 4 / 7274 (0.05%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Laryngeal squamous cell carcinoma | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 7274 (0.00%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Leiomyosarcoma | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Leiomyosarcoma metastatic | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lentigo maligna | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Leukaemia | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Lip and/or oral cavity cancer | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Lip squamous cell carcinoma | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lipoma | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lung adenocarcinoma | | | |

| | | | |
|---|-------------------|-------------------|--|
| subjects affected / exposed | 4 / 7274 (0.05%) | 6 / 7266 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 6 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 2 | |
| Lung adenocarcinoma metastatic | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Lung adenocarcinoma stage I | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lung adenocarcinoma stage IV | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Lung cancer metastatic | | | |
| subjects affected / exposed | 4 / 7274 (0.05%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 2 | 0 / 1 | |
| Lung carcinoma cell type unspecified stage IV | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 3 / 7266 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 2 | |
| Lung neoplasm | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lung neoplasm malignant | | | |
| subjects affected / exposed | 12 / 7274 (0.16%) | 12 / 7266 (0.17%) | |
| occurrences causally related to treatment / all | 1 / 12 | 0 / 12 | |
| deaths causally related to treatment / all | 0 / 4 | 0 / 3 | |
| Lung squamous cell carcinoma stage III | | | |

| | | | |
|---|------------------|-------------------|--|
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Lymphocytic leukaemia | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Malignant melanoma | | | |
| subjects affected / exposed | 6 / 7274 (0.08%) | 10 / 7266 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 7 | 0 / 10 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Malignant melanoma in situ | | | |
| subjects affected / exposed | 4 / 7274 (0.05%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Malignant neoplasm of ampulla of Vater | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Malignant neoplasm of renal pelvis | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Melanocytic naevus | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Meningeal neoplasm | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Meningioma | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Meningioma malignant | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metastases to bone | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Metastases to central nervous system | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | |
| Metastases to liver | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metastases to spine | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Metastatic bronchial carcinoma | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Metastatic malignant melanoma | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Metastatic renal cell carcinoma | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metastatic squamous cell carcinoma | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metastatic uterine cancer | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mucinous adenocarcinoma of appendix | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myelodysplastic syndrome | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 3 / 7266 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Nasal cavity cancer | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nasopharyngeal cancer | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neoplasm recurrence | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neuroendocrine carcinoma metastatic | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neuroendocrine tumour | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neurofibroma | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Non-Hodgkin's lymphoma | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 6 / 7266 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 2 | |
| Non-small cell lung cancer | | | |
| subjects affected / exposed | 2 / 7274 (0.03%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Non-small cell lung cancer metastatic | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Oesophageal adenocarcinoma | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 2 | |
| Oesophageal carcinoma | | | |
| subjects affected / exposed | 3 / 7274 (0.04%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Oesophageal squamous cell carcinoma | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 2 / 7274 (0.03%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oropharyngeal squamous cell carcinoma | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Ovarian adenoma | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ovarian cancer | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ovarian cancer metastatic | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Ovarian germ cell teratoma benign | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ovarian granulosa-theca cell tumour | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ovarian neoplasm | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancreatic carcinoma | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 7 / 7274 (0.10%) | 8 / 7266 (0.11%) | |
| occurrences causally related to treatment / all | 2 / 7 | 0 / 8 | |
| deaths causally related to treatment / all | 2 / 6 | 0 / 4 | |
| Pancreatic carcinoma metastatic | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Papillary thyroid cancer | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Parathyroid tumour benign | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Penile cancer | | | |
| subjects affected / exposed | 2 / 7274 (0.03%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Penile squamous cell carcinoma | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Phaeochromocytoma | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pituitary tumour | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pituitary tumour benign | | | |

| | | | |
|---|-------------------|-------------------|--|
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Plasma cell myeloma | | | |
| subjects affected / exposed | 6 / 7274 (0.08%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Plasmablastic lymphoma | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Plasmacytoma | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pleomorphic liposarcoma | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pleural mesothelioma | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Polycythaemia vera | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (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 | 45 / 7274 (0.62%) | 36 / 7266 (0.50%) | |
| occurrences causally related to treatment / all | 0 / 45 | 0 / 36 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Prostate cancer metastatic | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 5 / 7274 (0.07%) | 5 / 7266 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 3 | 0 / 2 | |
| Prostate cancer recurrent | | | |
| subjects affected / exposed | 2 / 7274 (0.03%) | 3 / 7266 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Prostate cancer stage I | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Prostatic adenoma | | | |
| subjects affected / exposed | 2 / 7274 (0.03%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rectal adenocarcinoma | | | |
| subjects affected / exposed | 2 / 7274 (0.03%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Rectal cancer | | | |
| subjects affected / exposed | 4 / 7274 (0.05%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rectal cancer metastatic | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rectosigmoid cancer | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Renal cancer | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 3 / 7274 (0.04%) | 7 / 7266 (0.10%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 7 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal cancer metastatic | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal cell carcinoma | | | |
| subjects affected / exposed | 2 / 7274 (0.03%) | 3 / 7266 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal cell carcinoma recurrent | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal cell carcinoma stage I | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal cell carcinoma stage III | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal neoplasm | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal oncocytoma | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Retroperitoneal cancer | | | |

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|---|-------------------|-------------------|--|
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sarcoma | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin cancer | | | |
| subjects affected / exposed | 3 / 7274 (0.04%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Small cell lung cancer | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Squamous cell carcinoma | | | |
| subjects affected / exposed | 38 / 7274 (0.52%) | 26 / 7266 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 44 | 0 / 38 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Squamous cell carcinoma of head and neck | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (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 of lung | | | |
| subjects affected / exposed | 7 / 7274 (0.10%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 7 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Squamous cell carcinoma of skin | | | |
| subjects affected / exposed | 20 / 7274 (0.27%) | 12 / 7266 (0.17%) | |
| occurrences causally related to treatment / all | 0 / 23 | 0 / 13 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Squamous cell carcinoma of the oral cavity | | | |

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|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Squamous cell carcinoma of the tongue | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| T-cell lymphoma | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| T-cell prolymphocytic leukaemia | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Testis cancer | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thymic cancer metastatic | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thyroid adenoma | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thyroid cancer | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tongue cancer recurrent | | | |

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|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tongue neoplasm malignant stage unspecified | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tonsil cancer | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tonsil cancer metastatic | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Tracheal cancer | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tracheal neoplasm | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Transitional cell carcinoma | | | |
| subjects affected / exposed | 7 / 7274 (0.10%) | 7 / 7266 (0.10%) | |
| occurrences causally related to treatment / all | 0 / 7 | 0 / 8 | |
| deaths causally related to treatment / all | 0 / 2 | 0 / 1 | |
| Urethral neoplasm | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Uterine cancer | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 4 / 7274 (0.05%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Uterine leiomyoma | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| Angiodysplasia | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Aortic dissection | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (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 / 7274 (0.01%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Arterial haemorrhage | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Arteriovenous fistula | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bleeding varicose vein | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Deep vein thrombosis | | | |

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|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Femoral artery aneurysm | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haematoma | | | |
| subjects affected / exposed | 2 / 7274 (0.03%) | 6 / 7266 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypotension | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intra-abdominal haematoma | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lymphocele | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lymphoedema | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lymphorrhoea | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Temporal arteritis | | | |

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|--|------------------|------------------|--|
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Varicose vein | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Adverse drug reaction | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 3 / 7266 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Asthenia | | | |
| subjects affected / exposed | 3 / 7274 (0.04%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chest pain | | | |
| subjects affected / exposed | 8 / 7274 (0.11%) | 6 / 7266 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 8 | 0 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Device dislocation | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Device malfunction | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Drug intolerance | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fat necrosis | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fatigue | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gait disturbance | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Generalised oedema | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Granuloma | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hernia | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Malaise | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mucosal hyperaemia | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Multi-organ failure | | | |

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|---|-------------------|-------------------|--|
| subjects affected / exposed | 0 / 7274 (0.00%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 26 / 7274 (0.36%) | 17 / 7266 (0.23%) | |
| occurrences causally related to treatment / all | 0 / 31 | 0 / 19 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Puncture site haemorrhage | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal pain | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Submandibular mass | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Immune system disorders | | | |
| Corneal graft rejection | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Drug hypersensitivity | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Reproductive system and breast disorders | | | |

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|---|-------------------|-------------------|--|
| Atrophic vulvovaginitis | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Benign prostatic hyperplasia | | | |
| subjects affected / exposed | 11 / 7274 (0.15%) | 15 / 7266 (0.21%) | |
| occurrences causally related to treatment / all | 0 / 11 | 0 / 15 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Calculus prostatic | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cervical polyp | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Epididymal cyst | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Epididymitis | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Genital rash | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metrorrhagia | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Orchitis noninfective | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ovarian cyst | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pelvic floor muscle weakness | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Postmenopausal haemorrhage | | | |
| subjects affected / exposed | 2 / 7274 (0.03%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Prostatic obstruction | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Prostatism | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Prostatitis | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Prostatomegaly | | | |
| subjects affected / exposed | 3 / 7274 (0.04%) | 4 / 7266 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Uterine polyp | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Uterovaginal prolapse | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| 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 | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute pulmonary oedema | | | |
| subjects affected / exposed | 3 / 7274 (0.04%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Acute respiratory distress syndrome | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Acute respiratory failure | | | |
| subjects affected / exposed | 5 / 7274 (0.07%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Alveolitis | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Alveolitis allergic | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Asthma | | | |

| | | | |
|---|-------------------|-------------------|--|
| subjects affected / exposed | 4 / 7274 (0.05%) | 8 / 7266 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 10 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atelectasis | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchiectasis | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 30 / 7274 (0.41%) | 13 / 7266 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 37 | 0 / 18 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Chronic respiratory disease | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cough | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dyspnoea | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Emphysema | | | |
| subjects affected / exposed | 3 / 7274 (0.04%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Epistaxis | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 6 / 7274 (0.08%) | 9 / 7266 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 9 | 0 / 9 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemoptysis | | | |
| subjects affected / exposed | 2 / 7274 (0.03%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemothorax | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hydrothorax | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyperventilation | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypoxia | | | |
| subjects affected / exposed | 2 / 7274 (0.03%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Idiopathic pulmonary fibrosis | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Interstitial lung disease | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Laryngeal cyst | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lung disorder | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Nasal obstruction | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (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 | 2 / 7274 (0.03%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Orthopnoea | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pleural effusion | | | |
| subjects affected / exposed | 2 / 7274 (0.03%) | 4 / 7266 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pleuritic pain | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumothorax | | | |
| subjects affected / exposed | 4 / 7274 (0.05%) | 3 / 7266 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Productive cough | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (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 | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary arterial hypertension | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary fibrosis | | | |
| subjects affected / exposed | 2 / 7274 (0.03%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Pulmonary hypertension | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary oedema | | | |
| subjects affected / exposed | 2 / 7274 (0.03%) | 3 / 7266 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory distress | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| 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 | 0 / 7274 (0.00%) | 4 / 7266 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Sinus polyp | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (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 / 7274 (0.00%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Stridor | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tracheal disorder | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| Alcohol abuse | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (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 | 3 / 7274 (0.04%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Delirium | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Depression | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 3 / 7274 (0.04%) | 4 / 7266 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dissociative disorder | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Drug abuse | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Drug dependence | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Major depression | | | |
| subjects affected / exposed | 3 / 7274 (0.04%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mental status changes | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nicotine dependence | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Paranoid personality disorder | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Suicidal ideation | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 7274 (0.00%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Suicide attempt | | | |
| subjects affected / exposed | 2 / 7274 (0.03%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Investigations | | | |
| Anticoagulation drug level increased | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| 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 | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatic enzyme abnormal | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatic enzyme increased | | | |
| subjects affected / exposed | 2 / 7274 (0.03%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| International normalised ratio increased | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Prostatic specific antigen increased | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| White blood cell count increased | | | |

| | | | |
|---|-------------------|-------------------|--|
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (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 | | | |
| Abdominal wound dehiscence | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Accidental overdose | | | |
| subjects affected / exposed | 19 / 7274 (0.26%) | 17 / 7266 (0.23%) | |
| occurrences causally related to treatment / all | 15 / 19 | 13 / 17 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Acetabulum fracture | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Alcohol poisoning | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ankle fracture | | | |
| subjects affected / exposed | 3 / 7274 (0.04%) | 6 / 7266 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Arthropod bite | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Arthropod sting | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Avulsion fracture | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Brain contusion | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 3 / 7266 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Burns second degree | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Burns third degree | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| 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 | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chemical burns of eye | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Comminuted fracture | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Concussion | | | |
| subjects affected / exposed | 4 / 7274 (0.05%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Contusion | | | |

| | | | |
|---|-------------------|------------------|--|
| subjects affected / exposed | 2 / 7274 (0.03%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Craniocerebral injury | | | |
| subjects affected / exposed | 3 / 7274 (0.04%) | 3 / 7266 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Delayed recovery from anaesthesia | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dislocation of vertebra | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| 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 | 4 / 7274 (0.05%) | 3 / 7266 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fall | | | |
| subjects affected / exposed | 9 / 7274 (0.12%) | 9 / 7266 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 9 | 0 / 9 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Femoral neck fracture | | | |
| subjects affected / exposed | 3 / 7274 (0.04%) | 5 / 7266 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Femur fracture | | | |
| subjects affected / exposed | 11 / 7274 (0.15%) | 7 / 7266 (0.10%) | |
| occurrences causally related to treatment / all | 0 / 11 | 0 / 7 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fibula fracture | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 7274 (0.01%) | 3 / 7266 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Foot fracture | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 4 / 7266 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Forearm fracture | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Foreign body | | | |
| subjects affected / exposed | 2 / 7274 (0.03%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fracture | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fracture displacement | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal stoma complication | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hand fracture | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Head injury | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 2 / 7274 (0.03%) | 5 / 7266 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Heat stroke | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hip fracture | | | |
| subjects affected / exposed | 6 / 7274 (0.08%) | 5 / 7266 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Humerus fracture | | | |
| subjects affected / exposed | 9 / 7274 (0.12%) | 4 / 7266 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 9 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Incisional hernia | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intentional overdose | | | |
| subjects affected / exposed | 2 / 7274 (0.03%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 2 / 2 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Joint dislocation | | | |
| subjects affected / exposed | 2 / 7274 (0.03%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Laceration | | | |
| subjects affected / exposed | 2 / 7274 (0.03%) | 4 / 7266 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ligament injury | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ligament rupture | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 3 / 7266 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ligament sprain | | | |
| subjects affected / exposed | 2 / 7274 (0.03%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Limb traumatic amputation | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lower limb fracture | | | |
| subjects affected / exposed | 2 / 7274 (0.03%) | 4 / 7266 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lumbar vertebral fracture | | | |
| subjects affected / exposed | 2 / 7274 (0.03%) | 3 / 7266 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Meniscus injury | | | |
| subjects affected / exposed | 2 / 7274 (0.03%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mouth injury | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Muscle injury | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Near drowning | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Overdose | | | |
| subjects affected / exposed | 2 / 7274 (0.03%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Patella fracture | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pelvic fracture | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Periorbital haematoma | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Periprosthetic fracture | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Periprosthetic osteolysis | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Post procedural fistula | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Post procedural haemorrhage | | | |
| subjects affected / exposed | 3 / 7274 (0.04%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Postoperative ileus | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Postoperative wound complication | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Prescribed overdose | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Procedural complication | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pubis fracture | | | |
| subjects affected / exposed | 2 / 7274 (0.03%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary contusion | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Radius fracture | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 3 / 7274 (0.04%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal haematoma | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rib fracture | | | |
| subjects affected / exposed | 5 / 7274 (0.07%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Road traffic accident | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 5 / 7266 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skull fracture | | | |
| subjects affected / exposed | 3 / 7274 (0.04%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Soft tissue injury | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal column injury | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal compression fracture | | | |
| subjects affected / exposed | 4 / 7274 (0.05%) | 5 / 7266 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 5 | 1 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Splinter | | | |

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|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sternal fracture | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| 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 | 4 / 7274 (0.05%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Subdural haemorrhage | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Tendon rupture | | | |
| subjects affected / exposed | 5 / 7274 (0.07%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Testicular injury | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thermal burn | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thoracic vertebral fracture | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tibia fracture | | | |

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|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 7274 (0.01%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tongue injury | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Toxicity to various agents | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 5 / 7266 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tracheal injury | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Traumatic intracranial haemorrhage | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ulnar nerve injury | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper limb fracture | | | |
| subjects affected / exposed | 3 / 7274 (0.04%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary bladder rupture | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular pseudoaneurysm | | | |

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|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Wrist fracture | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 4 / 7266 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Congenital, familial and genetic disorders | | | |
| Arteriovenous malformation | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hamartoma | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hydrocele | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Phimosis | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyloric stenosis | | | |
| subjects affected / exposed | 2 / 7274 (0.03%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Syringomyelia | | | |
| subjects affected / exposed | 2 / 7274 (0.03%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vitello-intestinal duct remnant | | | |

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|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Angina pectoris | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrioventricular block | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bradycardia | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cor pulmonale | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Coronary artery thrombosis | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Palpitations | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pericardial effusion | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sinus arrhythmia | | | |

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|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Acoustic neuritis | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Arachnoid cyst | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ataxia | | | |
| subjects affected / exposed | 2 / 7274 (0.03%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Basal ganglia haemorrhage | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| 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 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Carpal tunnel syndrome | | | |
| subjects affected / exposed | 2 / 7274 (0.03%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cauda equina syndrome | | | |
| subjects affected / exposed | 2 / 7274 (0.03%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Central nervous system lesion | | | |

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|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 7274 (0.01%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cervical cord compression | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cervical myelopathy | | | |
| subjects affected / exposed | 3 / 7274 (0.04%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cervical radiculopathy | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cervicobrachial syndrome | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cognitive disorder | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Complex partial seizures | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Convulsion | | | |
| subjects affected / exposed | 6 / 7274 (0.08%) | 5 / 7266 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cubital tunnel syndrome | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dementia | | | |
| subjects affected / exposed | 2 / 7274 (0.03%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dementia Alzheimer's type | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dizziness | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 7 / 7266 (0.10%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 7 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dizziness postural | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Encephalopathy | | | |
| subjects affected / exposed | 2 / 7274 (0.03%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Epilepsy | | | |
| subjects affected / exposed | 3 / 7274 (0.04%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Facial paresis | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemorrhage intracranial | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Headache | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypersomnia | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intracranial aneurysm | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Loss of consciousness | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lumbar radiculopathy | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 3 / 7266 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Migraine | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Monoplegia | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myasthenia gravis | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myasthenia gravis crisis | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myelopathy | | | |
| subjects affected / exposed | 2 / 7274 (0.03%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nerve compression | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nerve root compression | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorder | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neuralgia | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| 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 | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neuropathy peripheral | | | |

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|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Normal pressure hydrocephalus | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Parkinson's disease | | | |
| subjects affected / exposed | 3 / 7274 (0.04%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Partial seizures | | | |
| subjects affected / exposed | 3 / 7274 (0.04%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peripheral sensorimotor neuropathy | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Petit mal epilepsy | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Piriformis syndrome | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Posterior reversible encephalopathy syndrome | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Postictal state | | | |

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|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Radiculitis lumbosacral | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Retrograde amnesia | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sciatica | | | |
| subjects affected / exposed | 4 / 7274 (0.05%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sensory disturbance | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal cord disorder | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Subarachnoid haemorrhage | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Subdural effusion | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Syncope | | | |

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|---|-------------------|-------------------|--|
| subjects affected / exposed | 1 / 7274 (0.01%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thoracic outlet syndrome | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ulnar tunnel syndrome | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular dementia | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vertebrobasilar insufficiency | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vertigo CNS origin | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 23 / 7274 (0.32%) | 23 / 7266 (0.32%) | |
| occurrences causally related to treatment / all | 0 / 23 | 0 / 24 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anaemia vitamin B12 deficiency | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Autoimmune haemolytic anaemia | | | |

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|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemolytic anaemia | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemorrhagic anaemia | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (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 | 6 / 7274 (0.08%) | 6 / 7266 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lymphadenopathy mediastinal | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Microcytic anaemia | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neutropenia | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Normochromic normocytic anaemia | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pernicious anaemia | | | |

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|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ear and labyrinth disorders | | | |
| Deafness bilateral | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypoacusis | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Meniere's disease | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sudden hearing loss | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tinnitus | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vertigo | | | |
| subjects affected / exposed | 2 / 7274 (0.03%) | 4 / 7266 (0.06%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vertigo labyrinthine | | | |

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|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vertigo positional | | | |
| subjects affected / exposed | 2 / 7274 (0.03%) | 3 / 7266 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vestibular disorder | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Eye disorders | | | |
| Amaurosis fugax | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Angle closure glaucoma | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cataract | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Corneal degeneration | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dacryostenosis acquired | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Optic ischaemic neuropathy | | | |

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|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Retinal detachment | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Visual acuity reduced | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| 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 | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Abdominal discomfort | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (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 | 1 / 7274 (0.01%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abdominal hernia obstructive | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abdominal pain upper | | | |

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|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 7274 (0.00%) | 4 / 7266 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abdominal wall haematoma | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abnormal faeces | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anal fissure | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| 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 | 1 / 7274 (0.01%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ascites | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Change of bowel habit | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colitis | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colitis ischaemic | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 2 / 7274 (0.03%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colonic fistula | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colonic pseudo-obstruction | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Constipation | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 4 / 7266 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Crohn's disease | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diaphragmatic hernia | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diverticular perforation | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diverticulum | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diverticulum intestinal | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 7274 (0.01%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diverticulum intestinal haemorrhagic | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Duodenal polyp | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Duodenal ulcer | | | |
| subjects affected / exposed | 3 / 7274 (0.04%) | 5 / 7266 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Duodenal ulcer haemorrhage | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Duodenitis | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dyspepsia | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dysphagia | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Enterovesical fistula | | | |

| | | | |
|---|------------------|-------------------|--|
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (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 | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Faecaloma | | | |
| subjects affected / exposed | 2 / 7274 (0.03%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastric polyps | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastric ulcer | | | |
| subjects affected / exposed | 4 / 7274 (0.05%) | 3 / 7266 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastric ulcer haemorrhage | | | |
| subjects affected / exposed | 2 / 7274 (0.03%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastritis | | | |
| subjects affected / exposed | 2 / 7274 (0.03%) | 10 / 7266 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 10 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastritis erosive | | | |
| subjects affected / exposed | 4 / 7274 (0.05%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastritis haemorrhagic | | | |

| | | | |
|---|-------------------|-------------------|--|
| subjects affected / exposed | 1 / 7274 (0.01%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroduodenal ulcer | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroduodenitis haemorrhagic | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 12 / 7274 (0.16%) | 11 / 7266 (0.15%) | |
| occurrences causally related to treatment / all | 0 / 14 | 0 / 11 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal necrosis | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal ulcer | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal ulcer haemorrhage | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 9 / 7266 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 10 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haematochezia | | | |

| | | | |
|---|-------------------|-------------------|--|
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemorrhoids | | | |
| subjects affected / exposed | 5 / 7274 (0.07%) | 4 / 7266 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ileus | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ileus paralytic | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (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 | 11 / 7274 (0.15%) | 12 / 7266 (0.17%) | |
| occurrences causally related to treatment / all | 0 / 12 | 0 / 12 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Inguinal hernia, obstructive | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intestinal haemorrhage | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intestinal ischaemia | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| 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 | 2 / 7274 (0.03%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intestinal perforation | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (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 | 2 / 7274 (0.03%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intussusception | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Jejunal perforation | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Large intestinal stenosis | | | |
| subjects affected / exposed | 2 / 7274 (0.03%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Large intestine perforation | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| 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 | 2 / 7274 (0.03%) | 6 / 7266 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 2 | 1 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lower gastrointestinal haemorrhage | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 2 / 7274 (0.03%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mallory-Weiss syndrome | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Melaena | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Obstruction gastric | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oedema mouth | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oesophageal achalasia | | | |
| subjects affected / exposed | 2 / 7274 (0.03%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oesophageal food impaction | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oesophageal motility disorder | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oesophageal spasm | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oesophageal varices haemorrhage | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancreatic pseudocyst | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peptic ulcer | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peptic ulcer perforation | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Periodontal disease | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pharyngo-oesophageal diverticulum | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (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 | 3 / 7274 (0.04%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rectal polyp | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 3 / 7274 (0.04%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rectal prolapse | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Salivary gland calculus | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Small intestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Small intestinal obstruction | | | |
| subjects affected / exposed | 6 / 7274 (0.08%) | 8 / 7266 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 8 | 0 / 8 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Small intestinal perforation | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Small intestinal ulcer haemorrhage | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tongue disorder | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Umbilical hernia | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 2 / 7274 (0.03%) | 4 / 7266 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 6 / 7274 (0.08%) | 3 / 7266 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Varices oesophageal | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Volvulus | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Bile duct stone | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Biliary colic | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Biliary dyskinesia | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholecystitis | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholelithiasis | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Drug-induced liver injury | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gallbladder polyp | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatic cirrhosis | | | |
| subjects affected / exposed | 2 / 7274 (0.03%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatic congestion | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatic cyst | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| 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 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| 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 | 0 / 7274 (0.00%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatitis | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| 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 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatitis toxic | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Angioedema | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Decubitus ulcer | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dermatitis contact | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dermatitis psoriasiform | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Eczema asteatotic | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyperkeratosis | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lichen sclerosus | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pemphigoid | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pruritus | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rash | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Bladder outlet obstruction | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bladder stenosis | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Calculus bladder | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Calculus ureteric | | | |

| | | | |
|---|------------------|-------------------|--|
| subjects affected / exposed | 6 / 7274 (0.08%) | 6 / 7266 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 8 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Calculus urinary | | | |
| subjects affected / exposed | 4 / 7274 (0.05%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haematuria | | | |
| subjects affected / exposed | 6 / 7274 (0.08%) | 6 / 7266 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hydronephrosis | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 3 / 7266 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nephrolithiasis | | | |
| subjects affected / exposed | 9 / 7274 (0.12%) | 10 / 7266 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 11 | 0 / 10 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal artery stenosis | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal colic | | | |
| subjects affected / exposed | 4 / 7274 (0.05%) | 4 / 7266 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal cyst | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal failure | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal failure acute | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal impairment | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (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 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Stag horn calculus | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tubulointerstitial nephritis | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| 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 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urethral stenosis | | | |
| subjects affected / exposed | 4 / 7274 (0.05%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary bladder polyp | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary incontinence | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary retention | | | |
| subjects affected / exposed | 6 / 7274 (0.08%) | 4 / 7266 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 7 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Endocrine disorders | | | |
| Adrenocortical insufficiency acute | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Goitre | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyperthyroidism | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypothyroidism | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Inappropriate antidiuretic hormone secretion | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |

| | | | |
|---|------------------|------------------|--|
| Ankle impingement | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Arthralgia | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Arthritis | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Arthritis reactive | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Arthropathy | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Back pain | | | |
| subjects affected / exposed | 4 / 7274 (0.05%) | 6 / 7266 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bursitis | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chondrocalcinosis | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Compartment syndrome | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 7274 (0.01%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dupuytren's contracture | | | |
| subjects affected / exposed | 3 / 7274 (0.04%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gouty arthritis | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemarthrosis | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intervertebral disc compression | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intervertebral disc disorder | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intervertebral disc displacement | | | |
| subjects affected / exposed | 2 / 7274 (0.03%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intervertebral disc protrusion | | | |
| subjects affected / exposed | 8 / 7274 (0.11%) | 8 / 7266 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 8 | 0 / 9 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Joint effusion | | | |

| | | | |
|---|-------------------|-------------------|--|
| subjects affected / exposed | 1 / 7274 (0.01%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Joint swelling | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (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 | 5 / 7274 (0.07%) | 13 / 7266 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 14 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 6 / 7274 (0.08%) | 5 / 7266 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 3 / 7274 (0.04%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myalgia | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteitis | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteoarthritis | | | |
| subjects affected / exposed | 35 / 7274 (0.48%) | 52 / 7266 (0.72%) | |
| occurrences causally related to treatment / all | 0 / 37 | 0 / 54 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteochondrosis | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 2 / 7274 (0.03%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteoporosis | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Polymyalgia rheumatica | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psoriatic arthropathy | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rheumatoid arthritis | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 1 / 7266 (0.01%) | |
| 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 | 7 / 7274 (0.10%) | 6 / 7266 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 7 | 0 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal column stenosis | | | |
| subjects affected / exposed | 3 / 7274 (0.04%) | 4 / 7266 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal osteoarthritis | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 5 / 7274 (0.07%) | 7 / 7266 (0.10%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 7 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spondylolisthesis | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Synovial cyst | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tenosynovitis | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tenosynovitis stenosans | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Trigger finger | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Abdominal abscess | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Acute hepatitis B | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Appendicitis | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 2 / 7274 (0.03%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Appendicitis perforated | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchitis | | | |
| subjects affected / exposed | 4 / 7274 (0.05%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bursitis infective | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dengue fever | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diverticulitis | | | |
| subjects affected / exposed | 4 / 7274 (0.05%) | 6 / 7266 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 7 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis | | | |
| subjects affected / exposed | 2 / 7274 (0.03%) | 3 / 7266 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatitis C | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 3 / 7266 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatitis E | | | |

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|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Herpes simplex encephalitis | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Herpes zoster | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infected bites | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infective exacerbation of chronic obstructive airways disease | | | |
| subjects affected / exposed | 3 / 7274 (0.04%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Influenza | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Laryngitis | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Liver abscess | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lower respiratory tract infection | | | |

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|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lyme disease | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mycetoma mycotic | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oesophageal candidiasis | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteomyelitis | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Otitis media | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Otitis media chronic | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (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 | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary tuberculosis | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (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 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Scrub typhus | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sepsis | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sialoadenitis | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tooth abscess | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Typhoid fever | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urosepsis | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Viral infection | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Wound infection | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dehydration | | | |
| subjects affected / exposed | 8 / 7274 (0.11%) | 5 / 7266 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 8 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Electrolyte imbalance | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Failure to thrive | | | |
| subjects affected / exposed | 2 / 7274 (0.03%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyperkalaemia | | | |

| | | | |
|---|-------------------|------------------|--|
| subjects affected / exposed | 5 / 7274 (0.07%) | 8 / 7266 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 9 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypoalbuminaemia | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypochloraemia | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 2 / 7266 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypokalaemia | | | |
| subjects affected / exposed | 4 / 7274 (0.05%) | 3 / 7266 (0.04%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyponatraemia | | | |
| subjects affected / exposed | 21 / 7274 (0.29%) | 8 / 7266 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 21 | 0 / 9 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypophagia | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypophosphataemia | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypovolaemia | | | |
| subjects affected / exposed | 1 / 7274 (0.01%) | 0 / 7266 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Obesity | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 7274 (0.01%) | 1 / 7266 (0.01%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | Placebo | Sitagliptin | |
|---|------------------|------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 0 / 7274 (0.00%) | 0 / 7266 (0.00%) | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------------|--|
| 16 September 2010 | Amendment 1: Revised eligibility criteria to include participants on insulin and reduced the minimum number of participants to be recruited on pioglitazone (either as monotherapy or combination therapy) from 2000 to 1000. |
| 05 April 2012 | Amendment 2: The non-inferiority margin was revised from 1.20 to 1.30 to provide consistency with current regulatory guidance. |
| 25 September 2013 | Amendment 3: The secondary objective related to the analysis of each of the components of the primary composite endpoint was revised to include fatal myocardial infarctions and fatal strokes when analyzing the time to these individual categories of events. |
| 13 March 2014 | Amendment 4: The protocol was amended to allow for the collection of new or worsening malignancy and pancreatitis information beyond 28 days after discontinuation of study drug, and indicate that reported events of basal and/or squamous cell carcinoma of the skin will not undergo adjudication by the Clinical Events Classification Committee. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported