# Clinical trial results:
# A Randomized, Multicountry, Multicenter, Double-Blind, Parallel, Placebo-Controlled Study of the Effects of Atrasentan on Renal Outcomes in Subjects with Type 2 Diabetes and Nephropathy. SONAR: Study Of Diabetic Nephropathy with Atrasentan

## Summary

| | |
|---|---|
| EudraCT number | 2012-005848-21 |
| Trial protocol | SE DE CZ BE GB IE PT DK NL IT GR SK FI ES PL AT |
| Global end of trial date | 29 March 2018 |

### Results information

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 14 April 2019 |
| First version publication date | 14 April 2019 |

## Trial information

### Trial identification

| | |
|---|---|
| Sponsor protocol code | M11-352 |

### Additional study identifiers

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01858532 |
| WHO universal trial number (UTN) | - |

Notes:

### Sponsors

| | |
|---|---|
| Sponsor organisation name | AbbVie Deutschland GmbH & Co. KG |
| Sponsor organisation address | AbbVie House, Vanwall Business Park, Vanwall Road, Maidenhead, Berkshire, United Kingdom, SL6-4UB |
| Public contact | Global Medical Services, AbbVie, 001 800-633-9110, |
| Scientific contact | Melissa Wigderson, AbbVie, melissa.wigderson@abbvie.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 | 29 March 2018 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 29 March 2018 |
| Was the trial ended prematurely? | Yes |

Notes:

## General information about the trial

Main objective of the trial:

The study objective was to evaluate the effect of atrasentan compared with placebo on time to doubling of serum creatinine (DBSC) or the onset of end-stage renal disease (ESRD) in adults with type 2 diabetes and nephropathy who were treated with the maximum tolerated labeled daily dose (MTLDD) of a renin-angiotensin system (RAS) inhibitor. The study also assessed cardiovascular (CV) morbidity and mortality, urine albumin excretion, and changes in estimated glomerular filtration rate (eGFR). There was an optional Pre-Screening Period, Screening Period, Run-In Period (up to 12 weeks), Enrichment Period (6 weeks of atrasentan Tx), Double-Blind Treatment Period (randomization to final Tx visit), and Follow-Up Period (Final Tx to F1 visit [45 days post Tx] and other post-treatment visits). The study was prematurely discontinued because of a lower than expected event rate for the renal composite endpoint, which was adjudicated by a blinded independent events adjudication committee.

Protection of trial subjects:

Prior to the initiation of any screening or study-specific procedures, the investigator or his or her representative explained the nature of the study to the subject or his or her representative and answered all questions regarding this study.

| | |
|---|---|
| Background therapy: - | |
| Evidence for comparator: - | |
| Actual start date of recruitment | 17 May 2013 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Argentina: 62 |
| Country: Number of subjects enrolled | Australia: 56 |
| Country: Number of subjects enrolled | Austria: 14 |
| Country: Number of subjects enrolled | Belgium: 22 |
| Country: Number of subjects enrolled | Brazil: 259 |
| Country: Number of subjects enrolled | Canada: 74 |
| Country: Number of subjects enrolled | Chile: 40 |
| Country: Number of subjects enrolled | China: 283 |
| Country: Number of subjects enrolled | Czech Republic: 66 |
| Country: Number of subjects enrolled | Denmark: 28 |
| Country: Number of subjects enrolled | Finland: 12 |
| Country: Number of subjects enrolled | France: 48 |
| Country: Number of subjects enrolled | Germany: 79 |
| Country: Number of subjects enrolled | Greece: 38 |

| | |
|---|---|
| Country: Number of subjects enrolled | Hong Kong: 135 |
| Country: Number of subjects enrolled | Ireland: 25 |
| Country: Number of subjects enrolled | Israel: 82 |
| Country: Number of subjects enrolled | Italy: 166 |
| Country: Number of subjects enrolled | Japan: 386 |
| Country: Number of subjects enrolled | Korea, Republic of: 234 |
| Country: Number of subjects enrolled | Malaysia: 195 |
| Country: Number of subjects enrolled | Mexico: 149 |
| Country: Number of subjects enrolled | Netherlands: 41 |
| Country: Number of subjects enrolled | New Zealand: 45 |
| Country: Number of subjects enrolled | Peru: 111 |
| Country: Number of subjects enrolled | Poland: 56 |
| Country: Number of subjects enrolled | Portugal: 38 |
| Country: Number of subjects enrolled | Puerto Rico: 132 |
| Country: Number of subjects enrolled | Romania: 49 |
| Country: Number of subjects enrolled | Russian Federation: 164 |
| Country: Number of subjects enrolled | Singapore: 33 |
| Country: Number of subjects enrolled | Slovakia: 65 |
| Country: Number of subjects enrolled | South Africa: 64 |
| Country: Number of subjects enrolled | Spain: 315 |
| Country: Number of subjects enrolled | Sweden: 8 |
| Country: Number of subjects enrolled | Switzerland: 1 |
| Country: Number of subjects enrolled | Taiwan: 141 |
| Country: Number of subjects enrolled | Turkey: 19 |
| Country: Number of subjects enrolled | Ukraine: 111 |
| Country: Number of subjects enrolled | United Kingdom: 24 |
| Country: Number of subjects enrolled | United States: 1237 |
| Worldwide total number of subjects | 5107 |
| EEA total number of subjects | 1094 |

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) | 2473 |
| From 65 to 84 years | 2621 |
| 85 years and over | 13 |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

5107 participants dosed in the Enrichment Period (EP); 1441 prematurely discontinued Tx or did not proceed to the Double-Blind Treatment Period per criteria. 3666 participants completed EP and proceeded to Double-Blind Treatment Period, along with 2 additional participants who discontinued study drug in EP but were randomized in error.

### Period 1

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

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Intent-to-Treat (ITT) Responder atrasentan |

Arm description:

Participants who achieved at least 30% reduction in their albumin to creatinine ratio (UACR) in the Enrichment Period and were randomized to receive atrasentan in the Double-Blind Treatment Period

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Atrasentan |
| Investigational medicinal product code | |
| Other name | ABT-627 |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

0.75 mg atrasentan once daily by mouth for 48 months

| | |
|---|---|
| **Arm title** | Intent-to-Treat (ITT) Responder placebo |

Arm description:

Participants who achieved at least 30% reduction in their albumin to creatinine ratio (UACR) in the Enrichment Period and were randomized to receive placebo in the Double-Blind Treatment Period

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

Dosage and administration details:

Placebo once daily by mouth for 48 months

| | |
|---|---|
| **Arm title** | Intent-to-Treat (ITT) Non-responder atrasentan |

Arm description:

Participants who achieved < 30% reduction in their urinary albumin to creatinine ratio (UACR) in the Enrichment Period and were randomized to receive atrasentan in the Double-Blind Treatment Period

| | |
|---|---|
| Arm type | Experimental |

| | |
|---|---|
| Investigational medicinal product name | Atrasentan |
| Investigational medicinal product code | |
| Other name | ABT-627 |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

0.75 mg atrasentan once daily by mouth for 48 months

| | |
|---|---|
| **Arm title** | Intent-to-Treat (ITT) Non-responder placebo |

Arm description:

Participants who achieved < 30% reduction in their urinary albumin to creatinine ratio (UACR) in the Enrichment Period and were randomized to receive placebo in the Double-Blind Treatment Period

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

Dosage and administration details:

Placebo once daily by mouth for 48 months

| **Number of subjects in period 1[1]** | Intent-to-Treat (ITT) Responder atrasentan | Intent-to-Treat (ITT) Responder placebo | Intent-to-Treat (ITT) Non-responder atrasentan |
|---|---|---|---|
| Started | 1325 | 1323 | 509 |
| Completed | 1144 | 1131 | 411 |
| Not completed | 181 | 192 | 98 |
| Adverse event, non-fatal | 58 | 50 | 23 |
| Other, not specified | 29 | 15 | 13 |
| Withdrew consent | 71 | 93 | 46 |
| Lost to follow-up | 17 | 26 | 11 |
| Deterioration of medical status | 3 | 4 | 3 |
| Investigator request | 3 | 4 | 2 |

| **Number of subjects in period 1[1]** | Intent-to-Treat (ITT) Non-responder placebo |
|---|---|
| Started | 511 |
| Completed | 418 |
| Not completed | 93 |
| Adverse event, non-fatal | 28 |
| Other, not specified | 11 |
| Withdrew consent | 27 |
| Lost to follow-up | 14 |
| Deterioration of medical status | 7 |
| Investigator request | 6 |

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: 5107 subjects dosed in the open-label Enrichment Period (EP). Of these, 1441 either prematurely discontinued study treatment during the EP or were unable to proceed to the Double-Blind Treatment Period per protocol-specified criteria. 3,666 subjects completed the EP and proceeded into the Double-Blind Treatment Period, along with 2 additional subjects who discontinued study drug in the EP but were randomized in error, for a total of 3,668 subjects.

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Intent-to-Treat (ITT) Responder atrasentan |
| Reporting group description: | |
| Participants who achieved at least 30% reduction in their albumin to creatinine ratio (UACR) in the Enrichment Period and were randomized to receive atrasentan in the Double-Blind Treatment Period | |
| Reporting group title | Intent-to-Treat (ITT) Responder placebo |
| Reporting group description: | |
| Participants who achieved at least 30% reduction in their albumin to creatinine ratio (UACR) in the Enrichment Period and were randomized to receive placebo in the Double-Blind Treatment Period | |
| Reporting group title | Intent-to-Treat (ITT) Non-responder atrasentan |
| Reporting group description: | |
| Participants who achieved < 30% reduction in their urinary albumin to creatinine ratio (UACR) in the Enrichment Period and were randomized to receive atrasentan in the Double-Blind Treatment Period | |
| Reporting group title | Intent-to-Treat (ITT) Non-responder placebo |
| Reporting group description: | |
| Participants who achieved < 30% reduction in their urinary albumin to creatinine ratio (UACR) in the Enrichment Period and were randomized to receive placebo in the Double-Blind Treatment Period | |

| **Reporting group values** | Intent-to-Treat (ITT) Responder atrasentan | Intent-to-Treat (ITT) Responder placebo | Intent-to-Treat (ITT) Non-responder atrasentan |
|---|---|---|---|
| Number of subjects | 1325 | 1323 | 509 |
| Age categorical | | | |
| Units: Subjects | | | |
| Age continuous | | | |
| Intent-to-Treat (ITT) Responders (participants who achieved at least 30% reduction in their albumin to creatinine ratio (UACR) in the Enrichment Period [EP]) and ITT Non-responders (Participants who achieved < 30% reduction in their UACR in the EP) | | | |
| Units: years | | | |
| arithmetic mean | 64.9 | 64.7 | 63.8 |
| standard deviation | ± 8.64 | ± 8.66 | ± 9.12 |
| Gender categorical | | | |
| Intent-to-Treat (ITT) Responders (participants who achieved at least 30% reduction in their albumin to creatinine ratio (UACR) in the Enrichment Period [EP]) and ITT Non-responders (Participants who achieved < 30% reduction in their UACR in the EP) | | | |
| Units: Subjects | | | |
| Female | 331 | 352 | 127 |
| Male | 994 | 971 | 382 |

| **Reporting group values** | Intent-to-Treat (ITT) Non-responder placebo | Total | |
|---|---|---|---|
| Number of subjects | 511 | 3668 | |
| Age categorical | | | |
| Units: Subjects | | | |
| Age continuous | | | |
| Intent-to-Treat (ITT) Responders (participants who achieved at least 30% reduction in their albumin to creatinine ratio (UACR) in the Enrichment Period [EP]) and ITT Non-responders (Participants who achieved < 30% reduction in their UACR in the EP) | | | |

| | | | |
|---|---|---|---|
| Units: years | | | |
| arithmetic mean | 63.6 | | |
| standard deviation | ± 8.93 | - | |

| | | | |
|---|---|---|---|
| Gender categorical | | | |
| Intent-to-Treat (ITT) Responders (participants who achieved at least 30% reduction in their albumin to creatinine ratio (UACR) in the Enrichment Period [EP]) and ITT Non-responders (Participants who achieved < 30% reduction in their UACR in the EP) | | | |
| Units: Subjects | | | |
| Female | 136 | 946 | |
| Male | 375 | 2722 | |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Intent-to-Treat (ITT) Responder atrasentan |

Reporting group description:

Participants who achieved at least 30% reduction in their albumin to creatinine ratio (UACR) in the Enrichment Period and were randomized to receive atrasentan in the Double-Blind Treatment Period

| | |
|---|---|
| Reporting group title | Intent-to-Treat (ITT) Responder placebo |

Reporting group description:

Participants who achieved at least 30% reduction in their albumin to creatinine ratio (UACR) in the Enrichment Period and were randomized to receive placebo in the Double-Blind Treatment Period

| | |
|---|---|
| Reporting group title | Intent-to-Treat (ITT) Non-responder atrasentan |

Reporting group description:

Participants who achieved < 30% reduction in their urinary albumin to creatinine ratio (UACR) in the Enrichment Period and were randomized to receive atrasentan in the Double-Blind Treatment Period

| | |
|---|---|
| Reporting group title | Intent-to-Treat (ITT) Non-responder placebo |

Reporting group description:

Participants who achieved < 30% reduction in their urinary albumin to creatinine ratio (UACR) in the Enrichment Period and were randomized to receive placebo in the Double-Blind Treatment Period

| | |
|---|---|
| Subject analysis set title | Intent-to-Treat (ITT) Atrasentan |
| Subject analysis set type | Intention-to-treat |

Subject analysis set description:

All randomized participants who entered the Double-Blind Treatment Period and were randomized to receive atrasentan

| | |
|---|---|
| Subject analysis set title | Intent-to-Treat Placebo |
| Subject analysis set type | Intention-to-treat |

Subject analysis set description:

All randomized participants who entered the Double-Blind Treatment Period and were randomized to receive placebo

### Primary: Time to the first occurrence of a component of the composite renal endpoint in the Intent-to-Treat (ITT) Responder Set (as randomized)

| | |
|---|---|
| End point title | Time to the first occurrence of a component of the composite renal endpoint in the Intent-to-Treat (ITT) Responder Set (as randomized)[1] |

End point description:

Time to the first occurrence of a component of the composite renal endpoint was defined as doubling of serum creatinine (confirmed by a 30-day serum creatinine measurement) or the onset of end stage renal disease (estimated glomerular filtration rate [eGFR] less than 15 ml/min/1.73 m^2 confirmed by a 90-day eGFR measurement, receiving chronic dialysis, renal transplantation, or renal death). Only events adjudicated by the Events Adjudication Committee (EAC) were considered in defining this endpoint. Data are presented as number of participants with a primary renal composite event (first event per participant).

Analysis population: Intent-to-Treat (ITT) Responders (participants who achieved at least 30% reduction in their albumin to creatinine ratio [UACR] in the Enrichment Period [EP])

| | |
|---|---|
| End point type | Primary |

End point timeframe:

From randomization to individual end of observation, up to 53 months

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The Intent-to-Treat Responder Set (as randomized) is the primary analysis for this endpoint.

| **End point values** | Intent-to-Treat (ITT) Responder atrasentan | Intent-to-Treat (ITT) Responder placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1325 | 1323 | | |
| Units: Number of participants | 79 | 105 | | |

## Statistical analyses

| **Statistical analysis title** | Stratified log-rank test |
|---|---|

Statistical analysis description:

The endpoint was analyzed using the stratified log-rank test for treatment comparison.

| Comparison groups | Intent-to-Treat (ITT) Responder atrasentan v Intent-to-Treat (ITT) Responder placebo |
|---|---|
| Number of subjects included in analysis | 2648 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.029 |
| Method | Stratified log-rank test |

| **Statistical analysis title** | Cox Proportional Hazard Ratio |
|---|---|

Statistical analysis description:

A Cox Proportional Hazards regression model with pre-specified covariates adjusted was used to estimate the hazard ratio of atrasentan to placebo and its 95% confidence interval.

| Comparison groups | Intent-to-Treat (ITT) Responder atrasentan v Intent-to-Treat (ITT) Responder placebo |
|---|---|
| Number of subjects included in analysis | 2648 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.005 |
| Method | Regression, Cox |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.654 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.488 |
| upper limit | 0.878 |

## Secondary: Time to First Occurrence of a Component of Composite Renal Endpoint for All Randomized Participants (Pooled)

| End point title | Time to First Occurrence of a Component of Composite Renal Endpoint for All Randomized Participants (Pooled) |
|---|---|

End point description:

Time to the first occurrence of a component of the composite renal endpoint was defined as doubling of serum creatinine (confirmed by a 30-day serum creatinine measurement) or the onset of end stage renal disease (estimated glomerular filtration rate [eGFR] less than 15 ml/min/1.73 m^2 confirmed by a 90-day eGFR measurement, receiving chronic dialysis, renal transplantation, or renal death). Data for all randomized participants were pooled by treatment and analyzed. Data are presented as number of participants with a renal composite event (first event per participant).

Analysis Population: Intent-to-treat population: participants who were randomized to receive either atrasentan or placebo during the Double-Blind Treatment Period

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

End point timeframe:

From randomization to individual end of observation, up to 53 months

| **End point values** | Intent-to-Treat (ITT) Atrasentan | Intent-to-Treat Placebo | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 1834 | 1834 | | |
| Units: Number of participants | 152 | 192 | | |

### Statistical analyses

| **Statistical analysis title** | Cox Proportional Hazard Ratio |
|---|---|

Statistical analysis description:

A Cox Proportional Hazards regression model with pre-specified covariates adjusted was used to estimate the hazard ratio of atrasentan to placebo and its 95% confidence interval.

| Comparison groups | Intent-to-Treat Placebo v Intent-to-Treat (ITT) Atrasentan |
|---|---|
| Number of subjects included in analysis | 3668 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.002 |
| Method | Regression, Cox |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.72 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.58 |
| upper limit | 0.89 |

## Secondary: Time to Cardio-renal Composite Endpoint in the Intent-to-Treat (ITT) Responder Set (as randomized)

| End point title | Time to Cardio-renal Composite Endpoint in the Intent-to-Treat (ITT) Responder Set (as randomized)[2] |
|---|---|

End point description:

The composite event of interest for this outcome consisted of doubling of serum creatinine, end-stage renal disease (ESRD), cardiovascular (CV) death (including CV death and presumed CV death), nonfatal myocardial infarction (MI; heart attack) and nonfatal stroke. Presumed sudden cardiac death was included as a subcategory of presumed CV death. Only events adjudicated by the Events Adjudication Committee (EAC) were considered in defining this endpoint. Data are presented as number of participants with a cardio-renal composite event (first event per participant).

Analysis Population: Intent-to-Treat (ITT) Responders (participants who achieved at least 30% reduction in their albumin to creatinine ratio [UACR] in the Enrichment Period [EP])

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

End point timeframe:

From randomization to individual end of observation, up to 53 months

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The Intent-to-Treat Responder Set (as randomized) is the primary analysis for this endpoint.

| **End point values** | Intent-to-Treat (ITT) Responder atrasentan | Intent-to-Treat (ITT) Responder placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1325 | 1323 | | |
| Units: Number of participants | 147 | 172 | | |

### Statistical analyses

| **Statistical analysis title** | Stratified log-rank test |
|---|---|

Statistical analysis description:

The endpoint was analyzed using the stratified log-rank test for treatment comparison.

| Comparison groups | Intent-to-Treat (ITT) Responder atrasentan v Intent-to-Treat (ITT) Responder placebo |
|---|---|
| Number of subjects included in analysis | 2648 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.089 |
| Method | Stratified log-rank test |

| **Statistical analysis title** | Cox Proportional Hazard Ratio |
|---|---|

Statistical analysis description:

A Cox Proportional Hazards regression model with pre-specified covariates adjusted was used to estimate the hazard ratio of atrasentan to placebo and its 95% confidence interval.

| Comparison groups | Intent-to-Treat (ITT) Responder atrasentan v Intent-to-Treat |
|---|---|

| | (ITT) Responder placebo |
|---|---|
| Number of subjects included in analysis | 2648 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.049 |
| Method | Regression, Cox |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.801 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.642 |
| upper limit | 0.999 |

## Secondary: Time to a 50% Estimated Glomerular Filtration Rate Reduction in the Intent-to-Treat (ITT) Responder Set (as randomized)

| End point title | Time to a 50% Estimated Glomerular Filtration Rate Reduction in the Intent-to-Treat (ITT) Responder Set (as randomized)[3] |
|---|---|

End point description:

The event of interest for this outcome was a 50% reduction in a participant's estimated glomerular filtration rate (eGFR) value as compared to baseline, confirmed by a repeated value at least 20 days apart. The event time was defined as the first time that a 50% reduction in eGFR was observed. Data are presented as number of participants with a 50% reduction in eGFR (first event per participant).

Analysis Population Description
Intent-to-Treat (ITT) Responders (participants who achieved at least 30% reduction in their albumin to creatinine ratio [UACR] in the Enrichment Period [EP])

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

End point timeframe:

From randomization to individual end of observation, up to 53 months

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The Intent-to-Treat Responder Set (as randomized) is the primary analysis for this endpoint.

| **End point values** | Intent-to-Treat (ITT) Responder atrasentan | Intent-to-Treat (ITT) Responder placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1325 | 1323 | | |
| Units: Number of participants | 78 | 88 | | |

## Statistical analyses

| **Statistical analysis title** | Stratified log-rank test |
|---|---|

Statistical analysis description:

The endpoint was analyzed using the stratified log-rank test for treatment comparison.

| | |
|---|---|
| Comparison groups | Intent-to-Treat (ITT) Responder atrasentan v Intent-to-Treat (ITT) Responder placebo |
| Number of subjects included in analysis | 2648 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.289 |
| Method | Stratified log-rank test |

| **Statistical analysis title** | Cox Proportional Hazard Ratio |
|---|---|

Statistical analysis description:

A Cox Proportional Hazards regression model with pre-specified covariates adjusted was used to estimate the hazard ratio of atrasentan to placebo and its 95% confidence interval.

| Comparison groups | Intent-to-Treat (ITT) Responder atrasentan v Intent-to-Treat (ITT) Responder placebo |
|---|---|
| Number of subjects included in analysis | 2648 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.112 |
| Method | Regression, Cox |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.779 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.573 |
| upper limit | 1.06 |

## Secondary: Time to the Cardiovascular Composite Endpoint in the Intent-to-Treat (ITT) Responder Set (as randomized)

| End point title | Time to the Cardiovascular Composite Endpoint in the Intent-to-Treat (ITT) Responder Set (as randomized)[4] |
|---|---|

End point description:

The composite event of interest for this outcome was cardiovascular (CV) death (CV death, presumed CV death), nonfatal myocardial infarction (MI; heart attack), and nonfatal stroke. Presumed sudden cardiac death was included as a sub-category of presumed CV death. Only events adjudicated by the Events Adjudication Committee (EAC) were used. Data are presented as number of participants with a cardiovascular composite event (first event per participant).

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

End point timeframe:

From randomization to individual end of observation, up to 53 months

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The Intent-to-Treat Responder Set (as randomized) is the primary analysis for this endpoint.

| End point values | Intent-to-Treat (ITT) Responder atrasentan | Intent-to-Treat (ITT) Responder placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1325 | 1323 | | |
| Units: Number of participants | 72 | 81 | | |

## Statistical analyses

| Statistical analysis title | Stratified log-rank test |
|---|---|

Statistical analysis description:

The endpoint was analyzed using the stratified log-rank test for treatment comparison.

| Comparison groups | Intent-to-Treat (ITT) Responder atrasentan v Intent-to-Treat (ITT) Responder placebo |
|---|---|
| Number of subjects included in analysis | 2648 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.446 |
| Method | Stratified log-rank test |

| Statistical analysis title | Cox Proportional Hazard Ratio |
|---|---|

Statistical analysis description:

A Cox Proportional Hazards regression model with pre-specified covariates adjusted was used to estimate the hazard ratio of atrasentan to placebo and its 95% confidence interval.

| Comparison groups | Intent-to-Treat (ITT) Responder placebo v Intent-to-Treat (ITT) Responder atrasentan |
|---|---|
| Number of subjects included in analysis | 2648 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.447 |
| Method | Regression, Cox |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.884 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.643 |
| upper limit | 1.215 |

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Treatment-emergent adverse events (TEAEs) and serious adverse events (TESAEs) reported from time of study drug administration until 45 d after last dose (up to 24 wks for All Atrasentan Set in EP; 54 mos for ITT sets in Double-Blind period)

Adverse event reporting additional description:

TEAEs and TESAEs are defined as any adverse event (AE) with an onset date that is after the first dose of study drug until 45 days after the last dose of study drug and were collected whether elicited or spontaneously reported by the participant.

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

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 16.0 |

### Reporting groups

| | |
|---|---|
| Reporting group title | All Atrasentan Set |

Reporting group description:

Participants who received at least one dose of atrasentan, including both Enrichment and Double-Blind Treatment Periods

| | |
|---|---|
| Reporting group title | Double-Blind Placebo |

Reporting group description:

All participants who received at least one dose of placebo during the Double-Blind Treatment Period

| | |
|---|---|
| Reporting group title | Double-Blind Atrasentan |

Reporting group description:

All participants who received at least one dose of atrasentan during the Double-Blind Treatment Period

| Serious adverse events | All Atrasentan Set | Double-Blind Placebo | Double-Blind Atrasentan |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 292 / 5107 (5.72%) | 626 / 1830 (34.21%) | 685 / 1829 (37.45%) |
| number of deaths (all causes) | 25 | 79 | 84 |
| number of deaths resulting from adverse events | 23 | 64 | 65 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| ACUTE MYELOID LEUKAEMIA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| ADENOCARCINOMA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|---|---|---|
| ADENOCARCINOMA GASTRIC | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ADENOCARCINOMA OF COLON | | | |
| subjects affected / exposed | 2 / 5107 (0.04%) | 1 / 1830 (0.05%) | 3 / 1829 (0.16%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ADENOCARCINOMA PANCREAS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ADRENAL NEOPLASM | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ATYPICAL FIBROXANTHOMA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| BASAL CELL CARCINOMA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| BENIGN NEOPLASM OF BLADDER | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| BENIGN NEOPLASM OF THYROID GLAND | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| BENIGN RENAL NEOPLASM | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| BILE DUCT CANCER | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| BLADDER CANCER | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 3 / 1830 (0.16%) | 3 / 1829 (0.16%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | 1 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| BLADDER CANCER RECURRENT | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| BLADDER CANCER STAGE I, WITH CANCER IN SITU | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| BLADDER NEOPLASM | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 3 / 1830 (0.16%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| BLADDER TRANSITIONAL CELL CARCINOMA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 3 / 1830 (0.16%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| BONE NEOPLASM | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| BRAIN NEOPLASM | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| BRAIN NEOPLASM BENIGN | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| BREAST CANCER | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| BREAST CANCER RECURRENT | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| BREAST NEOPLASM | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| BRONCHIAL CARCINOMA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CARCINOID TUMOUR PULMONARY | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CHOLANGIOCARCINOMA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 2 / 1830 (0.11%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| CHRONIC LYMPHOCYTIC LEUKAEMIA | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| COLON ADENOMA | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 1 / 1830 (0.05%) | 7 / 1829 (0.38%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 1 / 7 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| COLON CANCER | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 2 / 1830 (0.11%) | 3 / 1829 (0.16%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 1 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| COLON NEOPLASM | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| COLORECTAL CANCER | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DIFFUSE LARGE B-CELL LYMPHOMA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| GALLBLADDER CANCER METASTATIC | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| ENDOMETRIAL CANCER | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| GASTRIC ADENOMA | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| GASTRIC CANCER | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 6 / 1830 (0.33%) | 3 / 1829 (0.16%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 6 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| GLIOBLASTOMA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| GASTROINTESTINAL TRACT ADENOMA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HEPATIC CANCER | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| HEPATOCELLULAR CARCINOMA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 3 / 1830 (0.16%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HUERTHLE CELL CARCINOMA | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| INFLAMMATORY PSEUDOTUMOUR | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| INTESTINAL ADENOCARCINOMA | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| LANGERHANS CELL SARCOMA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| INTRADUCTAL PROLIFERATIVE BREAST LESION | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| LIPOSARCOMA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| LIPOMA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| LARYNGEAL SQUAMOUS CELL CARCINOMA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| LUNG ADENOCARCINOMA STAGE IV | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| LUNG ADENOCARCINOMA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| LUNG NEOPLASM MALIGNANT | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| LUNG NEOPLASM | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| LUNG CANCER METASTATIC | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| MALIGNANT PALATE NEOPLASM | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| LYMPHOMA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| METASTATIC CARCINOMA OF THE BLADDER | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| METASTATIC MALIGNANT MELANOMA | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| METASTATIC NEOPLASM | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| MUCINOUS ADENOCARCINOMA OF APPENDIX | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| NASOPHARYNGEAL CANCER | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| NEUROENDOCRINE CARCINOMA | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| OESOPHAGEAL CARCINOMA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| NEUROENDOCRINE TUMOUR OF THE LUNG | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| OESOPHAGEAL SQUAMOUS CELL CARCINOMA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| OROPHARYNGEAL NEOPLASM | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| OSTEOSARCOMA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| OVARIAN CANCER | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| OVARIAN ADENOMA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PITUITARY TUMOUR BENIGN | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PANCREATIC CARCINOMA METASTATIC | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| PANCREATIC CARCINOMA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PROSTATE CANCER | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 7 / 1830 (0.38%) | 3 / 1829 (0.16%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 7 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PLASMA CELL MYELOMA | | | |
| subjects affected / exposed | 2 / 5107 (0.04%) | 0 / 1830 (0.00%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| PROSTATE CANCER RECURRENT | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PSEUDOMYXOMA PERITONEI | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PROSTATIC ADENOMA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| RECTAL ADENOCARCINOMA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 3 / 1830 (0.16%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 4 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| RENAL CANCER | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| RENAL CELL CARCINOMA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| RENAL CANCER METASTATIC | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| RENAL ONCOCYTOMA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SINONASAL PAPILLOMA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SQUAMOUS CELL CARCINOMA | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SMALL CELL LUNG CANCER METASTATIC | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| SQUAMOUS CELL CARCINOMA OF THE HYPOPHARYNX | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| SQUAMOUS CELL CARCINOMA OF LUNG | | | |
| subjects affected / exposed | 2 / 5107 (0.04%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| SQUAMOUS CELL CARCINOMA OF THE ORAL CAVITY | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| TRANSITIONAL CELL CARCINOMA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| THYROID NEOPLASM | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| TRANSITIONAL CELL CARCINOMA RECURRENT | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|---|---|---|
| UTERINE LEIOMYOMA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |
| ANEURYSM | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| AORTIC ANEURYSM | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 2 / 1830 (0.11%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| AORTIC STENOSIS | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 3 / 1830 (0.16%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| AORTIC ANEURYSM RUPTURE | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| ARTERIOSCLEROSIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| ARTERIAL STENOSIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ARTERIAL DISORDER | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| BLOOD PRESSURE INADEQUATELY | | | |

| | | | |
|---|---|---|---|
| CONTROLLED | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ARTERITIS | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DIABETIC VASCULAR DISORDER | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DEEP VEIN THROMBOSIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 4 / 1830 (0.22%) | 4 / 1829 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 4 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DRY GANGRENE | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| EXTREMITY NECROSIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 3 / 1829 (0.16%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HAEMATOMA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HYPERTENSION | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 9 / 1830 (0.49%) | 9 / 1829 (0.49%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 9 | 0 / 9 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HYPERTENSIVE CRISIS | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 5107 (0.04%) | 4 / 1830 (0.22%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 1 / 2 | 1 / 4 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HYPERTENSIVE EMERGENCY | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HYPOVOLAEMIC SHOCK | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HYPOTENSION | | | |
| subjects affected / exposed | 4 / 5107 (0.08%) | 4 / 1830 (0.22%) | 4 / 1829 (0.22%) |
| occurrences causally related to treatment / all | 4 / 5 | 1 / 4 | 1 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PERIPHERAL ARTERIAL OCCLUSIVE DISEASE | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 7 / 1830 (0.38%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 10 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| MALIGNANT HYPERTENSION | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 2 / 1830 (0.11%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ORTHOSTATIC HYPOTENSION | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 2 / 1830 (0.11%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 2 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PERIPHERAL ARTERY STENOSIS | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 2 / 1830 (0.11%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PERIPHERAL ARTERY OCCLUSION | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PERIPHERAL ARTERY THROMBOSIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PERIPHERAL VASCULAR DISORDER | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 2 / 1830 (0.11%) | 3 / 1829 (0.16%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PERIPHERAL ISCHAEMIA | | | |
| subjects affected / exposed | 2 / 5107 (0.04%) | 2 / 1830 (0.11%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SHOCK HAEMORRHAGIC | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| PERIPHERAL VENOUS DISEASE | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SUBCLAVIAN ARTERY OCCLUSION | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| THROMBOPHLEBITIS | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| VASCULAR OCCLUSION | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| BRAIN DEATH | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| ASTHENIA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 2 / 1830 (0.11%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CHEST DISCOMFORT | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CHEST PAIN | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 4 / 1830 (0.22%) | 7 / 1829 (0.38%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 4 | 1 / 7 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CHILLS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DEATH | | | |
| subjects affected / exposed | 3 / 5107 (0.06%) | 4 / 1830 (0.22%) | 5 / 1829 (0.27%) |
| occurrences causally related to treatment / all | 2 / 3 | 0 / 4 | 1 / 5 |
| deaths causally related to treatment / all | 2 / 3 | 0 / 4 | 1 / 5 |
| DISEASE COMPLICATION | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| FACE OEDEMA | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| FATIGUE | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| FEELING ABNORMAL | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| GENERAL PHYSICAL HEALTH DETERIORATION | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| GENERALISED OEDEMA | | | |
| subjects affected / exposed | 2 / 5107 (0.04%) | 3 / 1830 (0.16%) | 3 / 1829 (0.16%) |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 3 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HYPOTHERMIA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| IMPAIRED HEALING | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 3 / 1829 (0.16%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| INFLUENZA LIKE ILLNESS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| MULTIPLE ORGAN DYSFUNCTION SYNDROME | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 5107 (0.00%) | 3 / 1830 (0.16%) | 5 / 1829 (0.27%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 4 |
| NECROSIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| NON-CARDIAC CHEST PAIN | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 3 / 1830 (0.16%) | 4 / 1829 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| OEDEMA PERIPHERAL | | | |
| subjects affected / exposed | 4 / 5107 (0.08%) | 3 / 1830 (0.16%) | 6 / 1829 (0.33%) |
| occurrences causally related to treatment / all | 3 / 4 | 3 / 3 | 3 / 6 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PERIPHERAL SWELLING | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PYREXIA | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 2 / 1830 (0.11%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SUDDEN CARDIAC DEATH | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| SUDDEN DEATH | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 5 / 1830 (0.27%) | 8 / 1829 (0.44%) |
| occurrences causally related to treatment / all | 0 / 1 | 2 / 5 | 1 / 8 |
| deaths causally related to treatment / all | 0 / 1 | 2 / 5 | 1 / 8 |
| SYSTEMIC INFLAMMATORY RESPONSE SYNDROME | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ULCER HAEMORRHAGE | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| VASCULAR STENT STENOSIS | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune system disorders | | | |
| ALLERGY TO ARTHROPOD BITE | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ANAPHYLACTIC SHOCK | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DRUG HYPERSENSITIVITY | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HYPERSENSITIVITY | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Social circumstances | | | |
| OVERWORK | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Reproductive system and breast | | | |

| | | | |
|---|---|---|---|
| disorders | | | |
| BENIGN PROSTATIC HYPERPLASIA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 7 / 1830 (0.38%) | 3 / 1829 (0.16%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 7 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| EPIDIDYMAL CYST | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| GYNAECOMASTIA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PROSTATITIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SCROTAL OEDEMA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| UTERINE PROLAPSE | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| ACUTE PULMONARY OEDEMA | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 6 / 1830 (0.33%) | 5 / 1829 (0.27%) |
| occurrences causally related to treatment / all | 0 / 1 | 2 / 6 | 3 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 2 | 1 / 2 |
| ACUTE RESPIRATORY DISTRESS SYNDROME | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ACUTE RESPIRATORY FAILURE | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 9 / 1830 (0.49%) | 11 / 1829 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 9 | 0 / 11 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ASPIRATION | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| ASTHMA | | | |
| subjects affected / exposed | 3 / 5107 (0.06%) | 3 / 1830 (0.16%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 3 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| BRONCHOSPASM | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CHRONIC OBSTRUCTIVE PULMONARY DISEASE | | | |
| subjects affected / exposed | 3 / 5107 (0.06%) | 6 / 1830 (0.33%) | 9 / 1829 (0.49%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 7 | 0 / 9 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| COUGH | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DYSPNOEA | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 3 / 1830 (0.16%) | 5 / 1829 (0.27%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | 2 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DYSPNOEA EXERTIONAL | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 5107 (0.02%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| EPISTAXIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HAEMOPTYSIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HAEMOTHORAX | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HYDROTHORAX | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HYPERCAPNIA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HYPOVENTILATION | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HYPOXIA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| INTERSTITIAL LUNG DISEASE | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 3 / 1829 (0.16%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 2 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| MEDIASTINAL CYST | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| OBSTRUCTIVE AIRWAYS DISORDER | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PLEURAL EFFUSION | | | |
| subjects affected / exposed | 2 / 5107 (0.04%) | 2 / 1830 (0.11%) | 7 / 1829 (0.38%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | 1 / 7 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PNEUMOMEDIASTINUM | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PNEUMONIA ASPIRATION | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 1 / 1830 (0.05%) | 6 / 1829 (0.33%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 6 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PNEUMOTHORAX | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PULMONARY CONGESTION | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PULMONARY EMBOLISM | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 5107 (0.04%) | 2 / 1830 (0.11%) | 4 / 1829 (0.22%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| PULMONARY HYPERTENSION | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PULMONARY MASS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PULMONARY OEDEMA | | | |
| subjects affected / exposed | 6 / 5107 (0.12%) | 4 / 1830 (0.22%) | 7 / 1829 (0.38%) |
| occurrences causally related to treatment / all | 1 / 6 | 0 / 5 | 2 / 7 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| RESPIRATORY ARREST | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| RESPIRATORY DISTRESS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 5 / 1829 (0.27%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| RESPIRATORY FAILURE | | | |
| subjects affected / exposed | 3 / 5107 (0.06%) | 8 / 1830 (0.44%) | 6 / 1829 (0.33%) |
| occurrences causally related to treatment / all | 0 / 3 | 1 / 8 | 0 / 6 |
| deaths causally related to treatment / all | 0 / 2 | 1 / 4 | 0 / 1 |
| RESTRICTIVE PULMONARY DISEASE | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SLEEP APNOEA SYNDROME | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| AGITATION | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ANXIETY | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| BIPOLAR DISORDER | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CONFUSIONAL STATE | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DELIRIUM | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DELUSIONAL DISORDER, SOMATIC TYPE | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DEPRESSION | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DISORIENTATION | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DRUG ABUSE | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| INSOMNIA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| MENTAL STATUS CHANGES | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| MAJOR DEPRESSION | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SUICIDAL IDEATION | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Product issues | | | |
| Device capturing issue | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Device dislocation | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |

| | | | |
|---|---|---|---|
| BILE DUCT STONE | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 3 / 1830 (0.16%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| BILIARY COLIC | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CHOLANGITIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 2 / 1830 (0.11%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CHOLECYSTITIS | | | |
| subjects affected / exposed | 2 / 5107 (0.04%) | 2 / 1830 (0.11%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CHOLECYSTITIS ACUTE | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 3 / 1830 (0.16%) | 6 / 1829 (0.33%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 6 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CHOLECYSTITIS CHRONIC | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CHOLELITHIASIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 3 / 1830 (0.16%) | 5 / 1829 (0.27%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DRUG-INDUCED LIVER INJURY | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| GALLBLADDER PERFORATION | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HEPATIC CIRRHOSIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HEPATIC LESION | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HEPATIC STEATOSIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HEPATITIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HEPATITIS ACUTE | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Investigations | | | |
| BLOOD ALKALINE PHOSPHATASE INCREASED | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| BLOOD BICARBONATE DECREASED | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| BLOOD CREATININE INCREASED | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 5107 (0.02%) | 7 / 1830 (0.38%) | 5 / 1829 (0.27%) |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 8 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| BLOOD GLUCOSE DECREASED | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| BLOOD POTASSIUM INCREASED | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| BLOOD UREA INCREASED | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| BRAIN NATRIURETIC PEPTIDE INCREASED | | | |
| subjects affected / exposed | 2 / 5107 (0.04%) | 0 / 1830 (0.00%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ELECTROCARDIOGRAM Q WAVE ABNORMAL | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| GLOMERULAR FILTRATION RATE DECREASED | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HAEMOGLOBIN DECREASED | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HELICOBACTER TEST POSITIVE | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HEPATIC ENZYME INCREASED | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| LIPASE INCREASED | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| INTRAOCULAR PRESSURE INCREASED | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PROSTATIC SPECIFIC ANTIGEN INCREASED | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PROTEIN URINE PRESENT | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 1 / 1830 (0.05%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| TROPONIN INCREASED | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 2 / 1830 (0.11%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| URINE CYTOLOGY ABNORMAL | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| WEIGHT INCREASED | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| ABDOMINAL INJURY | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ANKLE FRACTURE | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 2 / 1830 (0.11%) | 3 / 1829 (0.16%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ABDOMINAL WOUND DEHISCENCE | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| BRAIN CONTUSION | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| BLADDER INJURY | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| BURNS SECOND DEGREE | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CERVICAL VERTEBRAL FRACTURE | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CLAVICLE FRACTURE | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CONCUSSION | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 3 / 1830 (0.16%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CONTUSION | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 2 / 1830 (0.11%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CYSTITIS RADIATION | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CRANIOCEREBRAL INJURY | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DISLOCATION OF VERTEBRA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| FACIAL BONES FRACTURE | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 1 / 1830 (0.05%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| FALL | | | |
| subjects affected / exposed | 7 / 5107 (0.14%) | 5 / 1830 (0.27%) | 12 / 1829 (0.66%) |
| occurrences causally related to treatment / all | 0 / 7 | 0 / 6 | 0 / 12 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| FEMORAL NECK FRACTURE | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 5107 (0.00%) | 3 / 1830 (0.16%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| FIBULA FRACTURE | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| FEMUR FRACTURE | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 3 / 1830 (0.16%) | 3 / 1829 (0.16%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| FOOT FRACTURE | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 2 / 1830 (0.11%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| FOREIGN BODY IN GASTROINTESTINAL TRACT | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| GRAFT THROMBOSIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HAND FRACTURE | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HEAD INJURY | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 3 / 1830 (0.16%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HIP FRACTURE | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 5107 (0.00%) | 2 / 1830 (0.11%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HUMERUS FRACTURE | | | |
| subjects affected / exposed | 2 / 5107 (0.04%) | 2 / 1830 (0.11%) | 3 / 1829 (0.16%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ILIUM FRACTURE | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 2 / 1830 (0.11%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| INCISIONAL HERNIA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| INJURY | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| JAW FRACTURE | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| JOINT DISLOCATION | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| LACERATION | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| LIGAMENT SPRAIN | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 5107 (0.02%) | 1 / 1830 (0.05%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| LIMB INJURY | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| LIMB TRAUMATIC AMPUTATION | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| LISFRANC FRACTURE | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| LOWER LIMB FRACTURE | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 3 / 1829 (0.16%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| LUMBAR VERTEBRAL FRACTURE | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 4 / 1830 (0.22%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 4 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| MENISCUS INJURY | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| MULTIPLE FRACTURES | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| MUSCLE RUPTURE | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 5107 (0.02%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| OVERDOSE | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PANCREATIC LEAK | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PATELLA FRACTURE | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PELVIC FRACTURE | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 2 / 1830 (0.11%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| POST CONCUSSION SYNDROME | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| POST PROCEDURAL DISCHARGE | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| POST PROCEDURAL HAEMATOMA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| POST PROCEDURAL HAEMORRHAGE | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 5107 (0.02%) | 2 / 1830 (0.11%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| POST PROCEDURAL SWELLING | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| POSTOPERATIVE WOUND COMPLICATION | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PROCEDURAL PAIN | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PUBIS FRACTURE | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| RADIUS FRACTURE | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 2 / 1830 (0.11%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| RIB FRACTURE | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 3 / 1829 (0.16%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ROAD TRAFFIC ACCIDENT | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 1 / 1830 (0.05%) | 3 / 1829 (0.16%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| SPINAL COMPRESSION FRACTURE | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SKIN ABRASION | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SPINAL CORD INJURY CERVICAL | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SPINAL FRACTURE | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SUBARACHNOID HAEMORRHAGE | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SUBDURAL HAEMATOMA | | | |
| subjects affected / exposed | 2 / 5107 (0.04%) | 2 / 1830 (0.11%) | 3 / 1829 (0.16%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 3 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SUBDURAL HAEMORRHAGE | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| TENDON RUPTURE | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| THERMAL BURN | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| THORACIC VERTEBRAL FRACTURE | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| TIBIA FRACTURE | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 2 / 1830 (0.11%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| TOXICITY TO VARIOUS AGENTS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| TRAUMATIC FRACTURE | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| TRAUMATIC HAEMATOMA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| TRAUMATIC HAEMOTHORAX | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| TRAUMATIC LUNG INJURY | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ULNA FRACTURE | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ULNAR NERVE INJURY | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| URINARY RETENTION POSTOPERATIVE | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| VASCULAR PSEUDOANEURYSM | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 2 / 1830 (0.11%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| WOUND | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 3 / 1829 (0.16%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| WOUND COMPLICATION | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| WOUND DEHISCENCE | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| WOUND HAEMORRHAGE | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| WOUND NECROSIS | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Congenital, familial and genetic disorders | | | |
| GLUCOSE-6-PHOSPHATE DEHYDROGENASE DEFICIENCY | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| ACUTE CORONARY SYNDROME | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 2 / 1830 (0.11%) | 5 / 1829 (0.27%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 2 | 1 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ACUTE LEFT VENTRICULAR FAILURE | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 3 / 1830 (0.16%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 4 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ACUTE MYOCARDIAL INFARCTION | | | |
| subjects affected / exposed | 7 / 5107 (0.14%) | 28 / 1830 (1.53%) | 34 / 1829 (1.86%) |
| occurrences causally related to treatment / all | 1 / 7 | 1 / 29 | 4 / 40 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 4 | 0 / 2 |
| ADAMS-STOKES SYNDROME | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ANGINA PECTORIS | | | |
| subjects affected / exposed | 4 / 5107 (0.08%) | 10 / 1830 (0.55%) | 10 / 1829 (0.55%) |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 10 | 0 / 11 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ANGINA UNSTABLE | | | |
| subjects affected / exposed | 4 / 5107 (0.08%) | 3 / 1830 (0.16%) | 7 / 1829 (0.38%) |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 3 | 1 / 7 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|---|---|---|
| AORTIC VALVE STENOSIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ARRHYTHMIA SUPRAVENTRICULAR | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ARRHYTHMIA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| ARTERIOSCLEROSIS CORONARY ARTERY | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| ATRIAL FIBRILLATION | | | |
| subjects affected / exposed | 2 / 5107 (0.04%) | 10 / 1830 (0.55%) | 16 / 1829 (0.87%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 11 | 4 / 17 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ATRIAL FLUTTER | | | |
| subjects affected / exposed | 2 / 5107 (0.04%) | 2 / 1830 (0.11%) | 5 / 1829 (0.27%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | 2 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ATRIAL TACHYCARDIA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ATRIOVENTRICULAR BLOCK | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ATRIOVENTRICULAR BLOCK COMPLETE | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 5107 (0.02%) | 2 / 1830 (0.11%) | 7 / 1829 (0.38%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 2 | 0 / 7 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ATRIOVENTRICULAR BLOCK FIRST DEGREE | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ATRIOVENTRICULAR BLOCK SECOND DEGREE | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 1 / 1830 (0.05%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| BRADYARRHYTHMIA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| BRADYCARDIA | | | |
| subjects affected / exposed | 3 / 5107 (0.06%) | 2 / 1830 (0.11%) | 4 / 1829 (0.22%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 2 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| BUNDLE BRANCH BLOCK BILATERAL | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| BUNDLE BRANCH BLOCK RIGHT | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 2 / 1830 (0.11%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| BUNDLE BRANCH BLOCK LEFT | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CARDIAC ARREST | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 3 / 5107 (0.06%) | 5 / 1830 (0.27%) | 4 / 1829 (0.22%) |
| occurrences causally related to treatment / all | 1 / 3 | 1 / 5 | 1 / 4 |
| deaths causally related to treatment / all | 1 / 3 | 1 / 5 | 1 / 3 |
| CARDIAC FAILURE | | | |
| subjects affected / exposed | 5 / 5107 (0.10%) | 11 / 1830 (0.60%) | 19 / 1829 (1.04%) |
| occurrences causally related to treatment / all | 4 / 5 | 5 / 11 | 6 / 20 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| CARDIAC FAILURE ACUTE | | | |
| subjects affected / exposed | 4 / 5107 (0.08%) | 4 / 1830 (0.22%) | 5 / 1829 (0.27%) |
| occurrences causally related to treatment / all | 2 / 4 | 0 / 5 | 4 / 6 |
| deaths causally related to treatment / all | 1 / 2 | 0 / 1 | 1 / 1 |
| CARDIAC FAILURE CHRONIC | | | |
| subjects affected / exposed | 3 / 5107 (0.06%) | 2 / 1830 (0.11%) | 5 / 1829 (0.27%) |
| occurrences causally related to treatment / all | 2 / 3 | 1 / 2 | 1 / 5 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| CARDIAC FAILURE CONGESTIVE | | | |
| subjects affected / exposed | 22 / 5107 (0.43%) | 22 / 1830 (1.20%) | 37 / 1829 (2.02%) |
| occurrences causally related to treatment / all | 17 / 22 | 7 / 23 | 15 / 41 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 1 |
| CARDIO-RESPIRATORY ARREST | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 1 / 1830 (0.05%) | 3 / 1829 (0.16%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | 0 / 3 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 1 | 0 / 3 |
| CARDIOGENIC SHOCK | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| CARDIOMYOPATHY | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| CARDIOPULMONARY FAILURE | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| CARDIORENAL SYNDROME | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CARDIOVASCULAR DISORDER | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CHRONIC LEFT VENTRICULAR FAILURE | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CORONARY ARTERY DISEASE | | | |
| subjects affected / exposed | 6 / 5107 (0.12%) | 19 / 1830 (1.04%) | 29 / 1829 (1.59%) |
| occurrences causally related to treatment / all | 1 / 6 | 1 / 20 | 3 / 31 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| CORONARY ARTERY OCCLUSION | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 3 / 1830 (0.16%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CORONARY ARTERY STENOSIS | | | |
| subjects affected / exposed | 3 / 5107 (0.06%) | 2 / 1830 (0.11%) | 5 / 1829 (0.27%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 2 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CORONARY ARTERY THROMBOSIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| CYANOSIS | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DIASTOLIC DYSFUNCTION | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HYPERTENSIVE CARDIOMYOPATHY | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HYPERTENSIVE HEART DISEASE | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| ISCHAEMIC CARDIOMYOPATHY | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| LEFT VENTRICULAR FAILURE | | | |
| subjects affected / exposed | 3 / 5107 (0.06%) | 1 / 1830 (0.05%) | 4 / 1829 (0.22%) |
| occurrences causally related to treatment / all | 2 / 3 | 0 / 1 | 1 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| MITRAL VALVE INCOMPETENCE | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| MYOCARDIAL INFARCTION | | | |
| subjects affected / exposed | 7 / 5107 (0.14%) | 8 / 1830 (0.44%) | 13 / 1829 (0.71%) |
| occurrences causally related to treatment / all | 3 / 7 | 0 / 8 | 4 / 15 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 2 |
| MYOCARDIAL ISCHAEMIA | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 5107 (0.02%) | 4 / 1830 (0.22%) | 9 / 1829 (0.49%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 4 | 0 / 11 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PALPITATIONS | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 2 / 1830 (0.11%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PERICARDIAL EFFUSION | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 4 / 1829 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| SINOATRIAL BLOCK | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SINUS ARREST | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SINUS NODE DYSFUNCTION | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 2 / 1830 (0.11%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SUPRAVENTRICULAR TACHYCARDIA | | | |
| subjects affected / exposed | 2 / 5107 (0.04%) | 1 / 1830 (0.05%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| TACHYCARDIA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 2 / 1830 (0.11%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| VENTRICULAR EXTRASYSTOLES | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| VENTRICULAR FIBRILLATION | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| VENTRICULAR TACHYCARDIA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| ALTERED STATE OF CONSCIOUSNESS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ACUTE MOTOR AXONAL NEUROPATHY | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| APHASIA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| BALANCE DISORDER | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CAROTID ARTERY OCCLUSION | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| BRAIN STEM INFARCTION | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CAROTID ARTERY STENOSIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 3 / 1830 (0.16%) | 3 / 1829 (0.16%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 1 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CARPAL TUNNEL SYNDROME | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CEREBELLAR HAEMATOMA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CEREBELLAR INFARCTION | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CEREBRAL HAEMORRHAGE | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 2 / 1830 (0.11%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| CEREBRAL INFARCTION | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 8 / 1830 (0.44%) | 3 / 1829 (0.16%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 9 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| CEREBRAL ISCHAEMIA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CEREBRAL THROMBOSIS | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CEREBROVASCULAR ACCIDENT | | | |
| subjects affected / exposed | 5 / 5107 (0.10%) | 14 / 1830 (0.77%) | 13 / 1829 (0.71%) |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 14 | 0 / 14 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 1 |
| CEREBROVASCULAR DISORDER | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 2 / 1830 (0.11%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CERVICOBRACHIAL SYNDROME | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| COMA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| DEMENTIA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DIABETIC COMA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DIABETIC HYPERGLYCAEMIC COMA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DIABETIC HYPEROSMOLAR COMA | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DIABETIC NEUROPATHY | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DIZZINESS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 3 / 1830 (0.16%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| EMBOLIC CEREBRAL INFARCTION | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ENCEPHALOPATHY | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| FACIAL PARALYSIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HEADACHE | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HAEMORRHAGIC STROKE | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 3 / 1830 (0.16%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| HEMIPARESIS | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HYDROCEPHALUS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HYPERTENSIVE ENCEPHALOPATHY | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HYPOGLYCAEMIC SEIZURE | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ISCHAEMIC STROKE | | | |
| subjects affected / exposed | 3 / 5107 (0.06%) | 9 / 1830 (0.49%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 1 / 3 | 0 / 10 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 1 |
| ISCHAEMIC CEREBRAL INFARCTION | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| IVTH NERVE PARALYSIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| LACUNAR INFARCTION | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 2 / 1830 (0.11%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| LOSS OF CONSCIOUSNESS | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| LUMBAR RADICULOPATHY | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| METABOLIC ENCEPHALOPATHY | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| MIGRAINE | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| MONONEUROPATHY MULTIPLEX | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| MYELOPATHY | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| MYOCLONUS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| NEUROPATHY PERIPHERAL | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PARAESTHESIA | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PRESYNCOPE | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| QUADRIPLEGIA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| RADICULOPATHY | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SCIATICA | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SEIZURE | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 2 / 1830 (0.11%) | 4 / 1829 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 6 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SENILE DEMENTIA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SPINAL CORD DISORDER | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SPONDYLITIC MYELOPATHY | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| STATUS EPILEPTICUS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SYNCOPE | | | |
| subjects affected / exposed | 3 / 5107 (0.06%) | 11 / 1830 (0.60%) | 6 / 1829 (0.33%) |
| occurrences causally related to treatment / all | 1 / 3 | 0 / 11 | 0 / 6 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| THALAMIC INFARCTION | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| TRANSIENT ISCHAEMIC ATTACK | | | |
| subjects affected / exposed | 2 / 5107 (0.04%) | 7 / 1830 (0.38%) | 7 / 1829 (0.38%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 7 | 1 / 7 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| VASCULAR DEMENTIA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| ANAEMIA | | | |
| subjects affected / exposed | 7 / 5107 (0.14%) | 11 / 1830 (0.60%) | 27 / 1829 (1.48%) |
| occurrences causally related to treatment / all | 2 / 7 | 1 / 15 | 3 / 28 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ANAEMIA OF CHRONIC DISEASE | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| AUTOIMMUNE HAEMOLYTIC ANAEMIA | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| COAGULOPATHY | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DISSEMINATED INTRAVASCULAR COAGULATION | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HAEMORRHAGIC ANAEMIA | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 1 / 1830 (0.05%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| IRON DEFICIENCY ANAEMIA | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 2 / 1830 (0.11%) | 4 / 1829 (0.22%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 2 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| LEUKOCYTOSIS | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| MICROCYTIC ANAEMIA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| NEPHROGENIC ANAEMIA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| NEUTROPENIA | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| PANCYTOPENIA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| THROMBOCYTOPENIA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ear and labyrinth disorders | | | |
| MENIERE'S DISEASE | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| VERTIGO | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 7 / 1830 (0.38%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 7 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| VERTIGO POSITIONAL | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Eye disorders | | | |
| AGE-RELATED MACULAR DEGENERATION | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ANGLE CLOSURE GLAUCOMA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|---|---|---|
| BLINDNESS TRANSIENT | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CATARACT | | | |
| subjects affected / exposed | 3 / 5107 (0.06%) | 10 / 1830 (0.55%) | 19 / 1829 (1.04%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 12 | 0 / 19 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CATARACT DIABETIC | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CATARACT NUCLEAR | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CORNEAL EPITHELIUM DEFECT | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CORNEAL OPACITY | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DACRYOSTENOSIS ACQUIRED | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DIABETIC RETINOPATHY | | | |
| subjects affected / exposed | 2 / 5107 (0.04%) | 0 / 1830 (0.00%) | 3 / 1829 (0.16%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DIPLOPIA | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| EYE HAEMORRHAGE | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 1 / 1830 (0.05%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| EYELID PTOSIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| GLAUCOMA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 3 / 1829 (0.16%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| LAGOPHTHALMOS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| MACULAR FIBROSIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| MACULAR OEDEMA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| OPTIC ISCHAEMIC NEUROPATHY | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PERIORBITAL OEDEMA | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| RETINAL DETACHMENT | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 2 / 1830 (0.11%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| RETINAL HAEMORRHAGE | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| RETINOPATHY PROLIFERATIVE | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| RHEGMATOGENOUS RETINAL DETACHMENT | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| TRACTIONAL RETINAL DETACHMENT | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| VISUAL IMPAIRMENT | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| VITREOUS ADHESIONS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| VITREOUS HAEMORRHAGE | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 4 / 5107 (0.08%) | 5 / 1830 (0.27%) | 9 / 1829 (0.49%) |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 7 | 0 / 9 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| ABDOMINAL DISTENSION | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ABDOMINAL HERNIA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 2 / 1830 (0.11%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ABDOMINAL PAIN | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 2 / 1830 (0.11%) | 3 / 1829 (0.16%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ANAL INCONTINENCE | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ANORECTAL ULCER | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ASCITES | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CHRONIC GASTRITIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| COLITIS | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 5107 (0.00%) | 2 / 1830 (0.11%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| COLITIS ULCERATIVE | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CONSTIPATION | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DENTAL CARIES | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DIABETIC GASTROPARESIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DIABETIC GASTROPATHY | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DIARRHOEA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 3 / 1830 (0.16%) | 4 / 1829 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DIVERTICULUM | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DIVERTICULUM INTESTINAL HAEMORRHAGIC | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DUODENAL ULCER | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DUODENAL ULCER HAEMORRHAGE | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 2 / 1830 (0.11%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DUODENITIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DYSPHAGIA | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 2 / 1830 (0.11%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ENTEROVESICAL FISTULA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| EROSIVE DUODENITIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 2 / 1830 (0.11%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| GASTRIC DISORDER | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| GASTRIC FISTULA | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| GASTRIC MUCOSAL HYPERTROPHY | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| GASTRIC POLYPS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| GASTRIC ULCER | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 2 / 1830 (0.11%) | 3 / 1829 (0.16%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| GASTRIC ULCER HAEMORRHAGE | | | |
| subjects affected / exposed | 2 / 5107 (0.04%) | 3 / 1830 (0.16%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 3 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| GASTRITIS | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| GASTRITIS HAEMORRHAGIC | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| GASTROINTESTINAL HAEMORRHAGE | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 3 / 1830 (0.16%) | 6 / 1829 (0.33%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | 0 / 6 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| GASTROINTESTINAL MUCOSAL DISORDER | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| GASTROOESOPHAGEAL REFLUX DISEASE | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 2 / 1830 (0.11%) | 3 / 1829 (0.16%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HAEMORRHOIDS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HIATUS HERNIA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ILEUS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 2 / 1830 (0.11%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| IMPAIRED GASTRIC EMPTYING | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| INGUINAL HERNIA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 2 / 1830 (0.11%) | 3 / 1829 (0.16%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| INTESTINAL HAEMORRHAGE | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| INTESTINAL OBSTRUCTION | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 3 / 1829 (0.16%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| INTESTINAL PERFORATION | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| IRRITABLE BOWEL SYNDROME | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| LARGE INTESTINE PERFORATION | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| LARGE INTESTINE POLYP | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 2 / 1830 (0.11%) | 7 / 1829 (0.38%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 7 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| LOWER GASTROINTESTINAL HAEMORRHAGE | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 2 / 1830 (0.11%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| LYMPHOCYTIC OESOPHAGITIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| MELAENA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| NAUSEA | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 5107 (0.04%) | 1 / 1830 (0.05%) | 4 / 1829 (0.22%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| OBSTRUCTIVE PANCREATITIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 2 / 1830 (0.11%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| OESOPHAGEAL SPASM | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| OESOPHAGEAL ULCER HAEMORRHAGE | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| OESOPHAGITIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PANCREATIC DISORDER | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PANCREATITIS | | | |
| subjects affected / exposed | 2 / 5107 (0.04%) | 4 / 1830 (0.22%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 5 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| PANCREATITIS ACUTE | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 4 / 1830 (0.22%) | 5 / 1829 (0.27%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 4 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PEPTIC ULCER HAEMORRHAGE | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PEPTIC ULCER | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PROCTITIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| RECTAL HAEMORRHAGE | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| RECTAL ULCER HAEMORRHAGE | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| RECTAL POLYP | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SMALL INTESTINAL OBSTRUCTION | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| UMBILICAL HERNIA | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ULCERATIVE GASTRITIS | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| UPPER GASTROINTESTINAL HAEMORRHAGE | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 3 / 1830 (0.16%) | 5 / 1829 (0.27%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| VOMITING | | | |
| subjects affected / exposed | 3 / 5107 (0.06%) | 5 / 1830 (0.27%) | 7 / 1829 (0.38%) |
| occurrences causally related to treatment / all | 0 / 3 | 1 / 5 | 0 / 8 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| ACTINIC KERATOSIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ANGIOEDEMA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DIABETIC CHEIROARTHROPATHY | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DECUBITUS ULCER | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DIABETIC FOOT | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 10 / 1830 (0.55%) | 8 / 1829 (0.44%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 10 | 0 / 10 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ECZEMA | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| INGROWING NAIL | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PRURITUS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SKIN DISCOLOURATION | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SKIN ULCER | | | |
| subjects affected / exposed | 4 / 5107 (0.08%) | 3 / 1830 (0.16%) | 5 / 1829 (0.27%) |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 3 | 0 / 10 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| ACUTE KIDNEY INJURY | | | |
| subjects affected / exposed | 19 / 5107 (0.37%) | 36 / 1830 (1.97%) | 54 / 1829 (2.95%) |
| occurrences causally related to treatment / all | 3 / 20 | 7 / 40 | 4 / 56 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| AZOTAEMIA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 3 / 1829 (0.16%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| BLADDER STENOSIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CALCULUS URINARY | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CHRONIC KIDNEY DISEASE | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 13 / 1830 (0.71%) | 9 / 1829 (0.49%) |
| occurrences causally related to treatment / all | 1 / 1 | 2 / 13 | 0 / 11 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DIABETIC NEPHROPATHY | | | |
| subjects affected / exposed | 2 / 5107 (0.04%) | 10 / 1830 (0.55%) | 17 / 1829 (0.93%) |
| occurrences causally related to treatment / all | 1 / 2 | 1 / 11 | 1 / 23 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| END STAGE RENAL DISEASE | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 27 / 1830 (1.48%) | 19 / 1829 (1.04%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 30 | 1 / 20 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| GLOMERULONEPHRITIS MEMBRANOUS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HAEMATURIA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 2 / 1830 (0.11%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HAEMORRHAGE URINARY TRACT | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HYDRONEPHROSIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 2 / 1830 (0.11%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HYDROURETER | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| NEPHROLITHIASIS | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 1 / 1830 (0.05%) | 4 / 1829 (0.22%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 1 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| NEPHROPATHY TOXIC | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PROTEINURIA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| RENAL ARTERY STENOSIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 2 / 1830 (0.11%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| RENAL FAILURE | | | |
| subjects affected / exposed | 2 / 5107 (0.04%) | 5 / 1830 (0.27%) | 5 / 1829 (0.27%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 5 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| RENAL IMPAIRMENT | | | |
| subjects affected / exposed | 3 / 5107 (0.06%) | 13 / 1830 (0.71%) | 10 / 1829 (0.55%) |
| occurrences causally related to treatment / all | 1 / 3 | 0 / 14 | 1 / 11 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| URETERIC OBSTRUCTION | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| RENAL VASCULITIS | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| URETHRAL STENOSIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| URETEROLITHIASIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 2 / 1830 (0.11%) | 3 / 1829 (0.16%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| URINARY BLADDER POLYP | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| URINARY RETENTION | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 1 / 1830 (0.05%) | 5 / 1829 (0.27%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | 0 / 7 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| URINARY TRACT OBSTRUCTION | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Endocrine disorders | | | |
| GOITRE | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HYPERPARATHYROIDISM PRIMARY | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |

| | | | |
|---|---|---|---|
| ARTHRALGIA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 3 / 1830 (0.16%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ARTHRITIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 2 / 1830 (0.11%) | 4 / 1829 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ARTHROPATHY | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CHRONIC KIDNEY DISEASE-MINERAL AND BONE DISORDER | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CERVICAL SPINAL STENOSIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| BACK PAIN | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 4 / 1830 (0.22%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 4 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| COMPARTMENT SYNDROME | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| COSTOCHONDRITIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HAEMARTHROSIS | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| GOUTY ARTHRITIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 4 / 1830 (0.22%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 4 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| INTERVERTEBRAL DISC DEGENERATION | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| INTERVERTEBRAL DISC DISORDER | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| INTERVERTEBRAL DISC DISPLACEMENT | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| INTERVERTEBRAL DISC PROTRUSION | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 4 / 1830 (0.22%) | 4 / 1829 (0.22%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 4 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| LUMBAR SPINAL STENOSIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 3 / 1830 (0.16%) | 5 / 1829 (0.27%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| JOINT SWELLING | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| MENISCAL DEGENERATION | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| MOBILITY DECREASED | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| MUSCULAR WEAKNESS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 2 / 1830 (0.11%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| MYALGIA | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| MUSCULOSKELETAL CHEST PAIN | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 5 / 1830 (0.27%) | 3 / 1829 (0.16%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 5 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| NECK PAIN | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| NEUROPATHIC ARTHROPATHY | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 1 / 1830 (0.05%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| OSTEOARTHRITIS | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 16 / 1830 (0.87%) | 8 / 1829 (0.44%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 19 | 0 / 8 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| OSTEITIS | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| OSTEOPOROSIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PAIN IN EXTREMITY | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| POLYARTHRITIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| RHABDOMYOLYSIS | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ROTATOR CUFF SYNDROME | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SACROILIITIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SOFT TISSUE NECROSIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SPINAL COLUMN STENOSIS | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SPINAL INSTABILITY | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SPINAL LIGAMENT OSSIFICATION | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SPINAL OSTEOARTHRITIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 3 / 1829 (0.16%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SPONDYLITIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SPONDYLOLISTHESIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SYMPATHETIC POSTERIOR CERVICAL SYNDROME | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SYNOVIAL CYST | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SYNOVITIS | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| THORACIC SPINAL STENOSIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| TORTICOLLIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| ABDOMINAL ABSCESS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ABSCESS LIMB | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 6 / 1830 (0.33%) | 6 / 1829 (0.33%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 7 | 0 / 6 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ABSCESS SOFT TISSUE | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ACUTE SINUSITIS | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ANAL ABSCESS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| APPENDICITIS | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 5107 (0.04%) | 3 / 1830 (0.16%) | 3 / 1829 (0.16%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 3 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ARTERIOSCLEROTIC GANGRENE | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ARTHRITIS BACTERIAL | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 2 / 1830 (0.11%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ARTHRITIS INFECTIVE | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| BACTERAEMIA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| BACTERIAL DIARRHOEA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| BACTERIAL SEPSIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| BILIARY SEPSIS | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| BRAIN ABSCESS | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| BRONCHITIS | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 4 / 1830 (0.22%) | 9 / 1829 (0.49%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 4 | 0 / 9 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| BRONCHITIS BACTERIAL | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CAMPYLOBACTER GASTROENTERITIS | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CAMPYLOBACTER INFECTION | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CELLULITIS | | | |
| subjects affected / exposed | 5 / 5107 (0.10%) | 22 / 1830 (1.20%) | 14 / 1829 (0.77%) |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 24 | 0 / 15 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CELLULITIS GANGRENOUS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CHOLECYSTITIS INFECTIVE | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CLOSTRIDIAL SEPSIS | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CHRONIC TONSILLITIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CLOSTRIDIUM DIFFICILE INFECTION | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CLOSTRIDIUM DIFFICILE COLITIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CYSTITIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CYSTITIS KLEBSIELLA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DENGUE FEVER | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DEVICE RELATED INFECTION | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DIABETIC FOOT INFECTION | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 5107 (0.00%) | 2 / 1830 (0.11%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DIVERTICULITIS | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 4 / 1830 (0.22%) | 4 / 1829 (0.22%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 4 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DIABETIC GANGRENE | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 3 / 1830 (0.16%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| EMPHYSEMATOUS PYELONEPHRITIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ENDOCARDITIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 3 / 1829 (0.16%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ENDOPHTHALMITIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ENTERITIS INFECTIOUS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ENTEROBACTER INFECTION | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ERYSIPELAS | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 5107 (0.02%) | 3 / 1830 (0.16%) | 3 / 1829 (0.16%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | 1 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ENTEROCOCCAL INFECTION | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 2 / 1830 (0.11%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ESCHERICHIA INFECTION | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ESCHERICHIA BACTERAEMIA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ESCHERICHIA SEPSIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 2 / 1830 (0.11%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| ESCHERICHIA URINARY TRACT INFECTION | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| GANGRENE | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 7 / 1830 (0.38%) | 4 / 1829 (0.22%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 7 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| GAS GANGRENE | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| GASTROENTERITIS | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 5107 (0.02%) | 10 / 1830 (0.55%) | 8 / 1829 (0.44%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 10 | 0 / 8 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| GASTROENTERITIS VIRAL | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| GRAFT INFECTION | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HELICOBACTER INFECTION | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HEPATITIS B | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HEPATITIS C | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HERPES ZOSTER | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| INFECTED SKIN ULCER | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 1 / 1830 (0.05%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| INFECTION | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| INFECTIVE EXACERBATION OF BRONCHIECTASIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| INFLUENZA | | | |
| subjects affected / exposed | 2 / 5107 (0.04%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| INTERVERTEBRAL DISCITIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| JOINT ABSCESS | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| KLEBSIELLA INFECTION | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| LEPTOSPIROSIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| LIVER ABSCESS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| LOCALISED INFECTION | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 5107 (0.00%) | 2 / 1830 (0.11%) | 3 / 1829 (0.16%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| LOWER RESPIRATORY TRACT INFECTION | | | |
| subjects affected / exposed | 2 / 5107 (0.04%) | 1 / 1830 (0.05%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| LUNG INFECTION | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 3 / 1830 (0.16%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| MASTOIDITIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 2 / 1830 (0.11%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| MEDICAL DEVICE SITE INFECTION | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| MORGANELLA INFECTION | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| NASOPHARYNGITIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| NECROTISING FASCIITIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 2 / 1830 (0.11%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| NEUTROPENIC SEPSIS | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| NOSOCOMIAL INFECTION | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ORCHITIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| OSTEOMYELITIS | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 10 / 1830 (0.55%) | 9 / 1829 (0.49%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 11 | 0 / 11 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| OSTEOMYELITIS ACUTE | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 2 / 1830 (0.11%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| OSTEOMYELITIS CHRONIC | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| OTITIS EXTERNA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| OTITIS MEDIA ACUTE | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| OTITIS MEDIA CHRONIC | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PANCREATITIS BACTERIAL | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PAROTID ABSCESS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PERIODONTITIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PERIRECTAL ABSCESS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PERITONITIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 3 / 1830 (0.16%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| PERITONSILLAR ABSCESS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PHARYNGEAL ABSCESS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PILONIDAL CYST | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PNEUMONIA | | | |
| subjects affected / exposed | 14 / 5107 (0.27%) | 41 / 1830 (2.24%) | 54 / 1829 (2.95%) |
| occurrences causally related to treatment / all | 0 / 14 | 3 / 43 | 2 / 63 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 1 |
| PNEUMONIA BACTERIAL | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 4 / 1829 (0.22%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PNEUMONIA LEGIONELLA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PNEUMONIA PARAINFLUENZAE VIRAL | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PNEUMONIA PSEUDOMONAL | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PNEUMONIA STAPHYLOCOCCAL | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PNEUMONIA STREPTOCOCCAL | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PNEUMONIA VIRAL | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 5107 (0.02%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| POST PROCEDURAL CELLULITIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| POST PROCEDURAL INFECTION | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| POSTOPERATIVE ABSCESS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| POSTOPERATIVE WOUND INFECTION | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PROSTATIC ABSCESS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PROSTATITIS ESCHERICHIA COLI | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PSEUDOMONAS INFECTION | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PULMONARY TUBERCULOMA | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PYELONEPHRITIS | | | |
| subjects affected / exposed | 3 / 5107 (0.06%) | 4 / 1830 (0.22%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 4 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PYELONEPHRITIS ACUTE | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 4 / 1830 (0.22%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 4 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PYELONEPHRITIS CHRONIC | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| RESPIRATORY TRACT INFECTION | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 1 / 1830 (0.05%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| RHINITIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SEPSIS | | | |
| subjects affected / exposed | 4 / 5107 (0.08%) | 18 / 1830 (0.98%) | 16 / 1829 (0.87%) |
| occurrences causally related to treatment / all | 0 / 4 | 2 / 18 | 0 / 17 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 3 |
| SEPSIS SYNDROME | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SEPTIC EMBOLUS | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SEPTIC ENCEPHALOPATHY | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SEPTIC NECROSIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SEPTIC SHOCK | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 6 / 1830 (0.33%) | 5 / 1829 (0.27%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 6 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| SIALOADENITIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| STAPHYLOCOCCAL ABSCESS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| STAPHYLOCOCCAL BACTERAEMIA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| STAPHYLOCOCCAL SEPSIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| STREPTOCOCCAL BACTERAEMIA | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SYSTEMIC CANDIDA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| TOOTH ABSCESS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| TOXIC SHOCK SYNDROME | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| UPPER RESPIRATORY TRACT INFECTION | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| TUBERCULOSIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 2 / 1830 (0.11%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| URINARY TRACT INFECTION | | | |
| subjects affected / exposed | 6 / 5107 (0.12%) | 12 / 1830 (0.66%) | 21 / 1829 (1.15%) |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 15 | 1 / 21 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| URINARY TRACT INFECTION ENTEROCOCCAL | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| URINARY TRACT INFECTION BACTERIAL | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| UROSEPSIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 2 / 1830 (0.11%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| VIRAL INFECTION | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| VULVAL ABSCESS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| WOUND INFECTION | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 2 / 1830 (0.11%) | 3 / 1829 (0.16%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| WOUND SEPSIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| WOUND INFECTION STAPHYLOCOCCAL | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 0 / 1830 (0.00%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| DECREASED APPETITE | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CACHEXIA | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DEHYDRATION | | | |
| subjects affected / exposed | 7 / 5107 (0.14%) | 8 / 1830 (0.44%) | 11 / 1829 (0.60%) |
| occurrences causally related to treatment / all | 0 / 7 | 0 / 8 | 1 / 11 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DIABETES MELLITUS | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 4 / 1830 (0.22%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 4 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DIABETES MELLITUS INADEQUATE CONTROL | | | |
| subjects affected / exposed | 3 / 5107 (0.06%) | 7 / 1830 (0.38%) | 9 / 1829 (0.49%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 7 | 0 / 9 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DIABETIC KETOACIDOSIS | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 1 / 1830 (0.05%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DIABETIC KETOSIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DIABETIC METABOLIC DECOMPENSATION | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 3 / 1830 (0.16%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 5 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ELECTROLYTE IMBALANCE | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 2 / 1830 (0.11%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| FLUID OVERLOAD | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 5107 (0.04%) | 3 / 1830 (0.16%) | 9 / 1829 (0.49%) |
| occurrences causally related to treatment / all | 1 / 2 | 2 / 3 | 3 / 10 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| FLUID RETENTION | | | |
| subjects affected / exposed | 2 / 5107 (0.04%) | 0 / 1830 (0.00%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| GOUT | | | |
| subjects affected / exposed | 1 / 5107 (0.02%) | 2 / 1830 (0.11%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 3 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HYPERCALCAEMIA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HYPERGLYCAEMIA | | | |
| subjects affected / exposed | 2 / 5107 (0.04%) | 9 / 1830 (0.49%) | 8 / 1829 (0.44%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 11 | 1 / 8 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HYPERGLYCAEMIC HYPEROSMOLAR NONKETOTIC SYNDROME | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HYPERKALAEMIA | | | |
| subjects affected / exposed | 5 / 5107 (0.10%) | 16 / 1830 (0.87%) | 16 / 1829 (0.87%) |
| occurrences causally related to treatment / all | 1 / 6 | 3 / 19 | 2 / 18 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HYPERURICAEMIA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HYPOCALCAEMIA | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HYPOALBUMINAEMIA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HYPONATRAEMIA | | | |
| subjects affected / exposed | 2 / 5107 (0.04%) | 2 / 1830 (0.11%) | 3 / 1829 (0.16%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 2 | 2 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HYPOMAGNESAEMIA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HYPOGLYCAEMIA | | | |
| subjects affected / exposed | 13 / 5107 (0.25%) | 12 / 1830 (0.66%) | 22 / 1829 (1.20%) |
| occurrences causally related to treatment / all | 0 / 13 | 0 / 14 | 0 / 24 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HYPOVOLAEMIA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HYPOPHAGIA | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 0 / 1830 (0.00%) | 1 / 1829 (0.05%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| METABOLIC ACIDOSIS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 6 / 1830 (0.33%) | 5 / 1829 (0.27%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 6 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| OBESITY | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 2 / 1829 (0.11%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| TYPE 2 DIABETES MELLITUS | | | |
| subjects affected / exposed | 0 / 5107 (0.00%) | 1 / 1830 (0.05%) | 0 / 1829 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

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

| **Non-serious adverse events** | All Atrasentan Set | Double-Blind Placebo | Double-Blind Atrasentan |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 1781 / 5107 (34.87%) | 1038 / 1830 (56.72%) | 1043 / 1829 (57.03%) |
| Vascular disorders | | | |
| HYPERTENSION | | | |
| subjects affected / exposed | 78 / 5107 (1.53%) | 218 / 1830 (11.91%) | 158 / 1829 (8.64%) |
| occurrences (all) | 79 | 257 | 179 |
| Blood and lymphatic system disorders | | | |
| ANAEMIA | | | |
| subjects affected / exposed | 180 / 5107 (3.52%) | 127 / 1830 (6.94%) | 216 / 1829 (11.81%) |
| occurrences (all) | 183 | 138 | 241 |
| General disorders and administration site conditions | | | |
| OEDEMA PERIPHERAL | | | |
| subjects affected / exposed | 1148 / 5107 (22.48%) | 483 / 1830 (26.39%) | 534 / 1829 (29.20%) |
| occurrences (all) | 1273 | 666 | 765 |
| Gastrointestinal disorders | | | |
| DIARRHOEA | | | |
| subjects affected / exposed | 103 / 5107 (2.02%) | 103 / 1830 (5.63%) | 99 / 1829 (5.41%) |
| occurrences (all) | 108 | 110 | 116 |
| Musculoskeletal and connective tissue disorders | | | |
| BACK PAIN | | | |
| subjects affected / exposed | 61 / 5107 (1.19%) | 125 / 1830 (6.83%) | 88 / 1829 (4.81%) |
| occurrences (all) | 62 | 133 | 93 |
| Infections and infestations | | | |

| | | | |
|---|---|---|---|
| UPPER RESPIRATORY TRACT INFECTION | | | |
| subjects affected / exposed | 110 / 5107 (2.15%) | 114 / 1830 (6.23%) | 106 / 1829 (5.80%) |
| occurrences (all) | 114 | 140 | 131 |
| NASOPHARYNGITIS | | | |
| subjects affected / exposed | 145 / 5107 (2.84%) | 169 / 1830 (9.23%) | 180 / 1829 (9.84%) |
| occurrences (all) | 152 | 278 | 274 |
| URINARY TRACT INFECTION | | | |
| subjects affected / exposed | 50 / 5107 (0.98%) | 93 / 1830 (5.08%) | 93 / 1829 (5.08%) |
| occurrences (all) | 51 | 135 | 126 |
| Metabolism and nutrition disorders | | | |
| HYPERKALAEMIA | | | |
| subjects affected / exposed | 77 / 5107 (1.51%) | 143 / 1830 (7.81%) | 132 / 1829 (7.22%) |
| occurrences (all) | 77 | 165 | 159 |
| HYPERURICAEMIA | | | |
| subjects affected / exposed | 84 / 5107 (1.64%) | 105 / 1830 (5.74%) | 101 / 1829 (5.52%) |
| occurrences (all) | 85 | 106 | 105 |
| HYPOGLYCAEMIA | | | |
| subjects affected / exposed | 126 / 5107 (2.47%) | 120 / 1830 (6.56%) | 114 / 1829 (6.23%) |
| occurrences (all) | 189 | 212 | 193 |

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 08 October 2014 | • ESRD for primary endpoint: confirmed eGFR < 15 mL/min/1.73 m^2<br>• Other endpoints: Changed time to 30% eGFR reduction after 2 mos post-random to 50% eGFR reduction; change from Baseline (BL) to 24 mo post-random on UACR new endpoint; made time to first occurrence of component of composite renal endpoint new endpoint; added endpoints about vascular events and laser photocoagulations<br>• Inclusion criterion (IC) 3: antihyperglycemic meds and ACE inhibitor or angiotensin receptor blocker at least 4 wks prior to screening visit 2; latent autoimmune diabetes or insulin-treated w/o history of diabetic ketoacidosis who also have a negative anti-GAD test + an elevated post-prandial serum C-peptide level<br>• IC 5: serum albumin criteria ≥ 2.5 g/dL (25 g/L); serum K upper limit =6.0 mEq/L; upper limit of systolic BP =180 mmHg; eligible BP at any time during screening<br>• IC 7: remove acute kidney injury; subjects may not have a weight gain ≥ 3 kg AND brain natriuretic peptide (BNP) ≥ 300 pg/mL last visit of the enrichment period compared to BL<br>• IC 8: dual contraception acceptable forms<br>• Removed HbA1c IC<br>• Exclusion criterion (EC) 1: removed moderate edema and pulmonary edema; updated time frame from 6 mos to 4 wks prior to screening.<br>• EC 2: subject has history of pulmonary hypertension, pulmonary fibrosis or any lung disease requiring oxygen therapy (e.g., chronic obstructive pulmonary disease, emphysema)<br>• EC 15: include atrasentan use<br>• Removed EC for Hx of symptomatic hypotension, BMI, and pioglitazone<br>• Added EC 22: subjects considered to be clinically unstable regarding general, metabolic or CV health determined by investigator<br>• Removed UACR blind during Enrichment Period<br>• Revised randomization strategy for non-responder to distribute non-responder chronologically throughout study in 1:3 proportion to # of responders randomized<br>• Revised primary efficacy analysis from Cox proportional-hazard model analysis to stratified log-rank test |
| 11 February 2015 | • Updated HOMA-IR calculation for insulin resistance<br>• Removed allowance for repeat of serum creatinine at an unscheduled visit (s) after E5<br>• Clarified that if during the Double-Blind Treatment Period the subject discontinued study drug, the investigator should only re-start if it was medically appropriate<br>• Added statement regarding the maximum duration of atrasentan exposure and maximum atrasentan dose<br>• Updated the number of study sites to 800 – 900<br>• Added additional clarification regarding the randomization strategy of the non-responder arm |

| | |
|---|---|
| 19 May 2017 | • Updated figures throughout protocol: Revised number of subjects to be enrolled from 4,148 to 3,500; revised responders (UACR reduction ≥ 30% from Baseline) in the Study Diagram from 1,574 to 1,250; revised number of responders from 3,148 to 2,500; extended yearly treatment visits past T48<br>• Updated statistical methods: Sample size determination, definition of Baseline, primary efficacy analysis, derivation of safety endpoints, interim analysis<br>• Updated duration of the Double-Blind Treatment Period from 48 months to approximately 6 years<br>• Clarified exclusion criterion 19 to re-define premenopausal women are not eligible for study participation |

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

None reported