# Clinical trial results:
# A multicentre international randomized parallel group double-blind placebo-controlled clinical trial of EMPAgliflozin once daily to assess cardio-renal outcomes in patients with chronic KIDNEY disease

## Summary

| | |
|---|---|
| EudraCT number | 2017-002971-24 |
| Trial protocol | DE GB IT |
| Global end of trial date | |

**Results information**

| | |
|---|---|
| Result version number | v2 |
| This version publication date | 07 February 2025 |
| First version publication date | 16 July 2023 |
| Version creation reason | |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | 1245-0137 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03594110 |
| WHO universal trial number (UTN) | - |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | Boehringer Ingelheim |
| Sponsor organisation address | Binger Strasse 173, Ingelheim am Rhein, Germany, 55216 |
| Public contact | Boehringer Ingelheim, Call Center, Boehringer Ingelheim, 001 18002430127, clintriage.rdg@boehringer-ingelheim.com |
| Scientific contact | Boehringer Ingelheim, Call Center, Boehringer Ingelheim, 001 18002430127, clintriage.rdg@boehringer-ingelheim.com |

Notes:

**Paediatric regulatory details**

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

Notes:

## Results analysis stage

| | |
|---|---|
| Analysis stage | Interim |
| Date of interim/final analysis | 09 September 2022 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 05 July 2022 |
| Global end of trial reached? | No |

Notes:

## General information about the trial

Main objective of the trial:

The primary aim of this trial was to assess the effect of empagliflozin on time to kidney disease progression or cardiovascular (CV) death.
Key secondary aims were to assess the effect of empagliflozin on time to hospitalisation for heart failure (HHF) or CV death, occurrences of hospitalisations from any cause, and time to death from any cause.

Protection of trial subjects:

Only participants that met all the study inclusion and none of the exclusion criteria were to be entered in the study. All participants were free to withdraw from the clinical trial at any time for any reason given. Close monitoring of participants was adhered to throughout the trial conduct. An independent data monitoring committee assessed participant safety and the progress of the trial through review of unblinded data at specified intervals.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 01 February 2019 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Scientific research |
| Long term follow-up duration | 2 Years |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Canada: 488 |
| Country: Number of subjects enrolled | China: 986 |
| Country: Number of subjects enrolled | Germany: 1269 |
| Country: Number of subjects enrolled | Italy: 246 |
| Country: Number of subjects enrolled | Japan: 612 |
| Country: Number of subjects enrolled | Malaysia: 646 |
| Country: Number of subjects enrolled | United Kingdom: 1133 |
| Country: Number of subjects enrolled | United States: 1229 |
| Worldwide total number of subjects | 6609 |
| EEA total number of subjects | 1515 |

Notes:

### Subjects enrolled per age group

| | |
|---|---|
| In utero | 0 |
| Preterm newborn - gestational age < 37 | 0 |

| wk | |
|---|---|
| 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) | 3003 |
| From 65 to 84 years | 3473 |
| 85 years and over | 133 |

## Subject disposition

### Recruitment

Recruitment details:

Prior to randomisation, potentially eligible participants entered a placebo run-in period for about 8-12 weeks.
Thereafter, the participants were to receive treatment with empagliflozin or placebo until approximately 1070 first primary outcome events had occurred after randomisation (i.e. event-driven).

### Pre-assignment

Screening details:

Subjects were screened for eligibility prior to participation and attended a specialist site which ensured that they (the subjects) met all inclusion and none of the exclusion criteria. 8266 subjects were screened in this trial. Population of Trial Subjects tables are based on the Randomised set.

### Period 1

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

Blinding implementation details:

Participants, investigators and everyone involved in trial conduct or analysis or with any other interest in this double-blind trial (apart from the Data Monitoring Committee (DMC)) remained blinded with regard to the randomised treatment assignments.

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Placebo |

Arm description:

Patients with evidence of chronic kidney disease (CKD) at risk of kidney disease progression, with or without diagnosed diabetes mellitus administered orally once daily film-coated tablets of placebo to match empagliflozin.

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

Dosage and administration details:

One tablet once daily.

| | |
|---|---|
| **Arm title** | Empagliflozin 10 mg |

Arm description:

Patients with evidence of chronic kidney disease (CKD) at risk of kidney disease progression, with or without diagnosed diabetes mellitus administered orally once daily 10 milligram (mg) film-coated tablets of empagliflozin.

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

Dosage and administration details:

One tablet of 10 milligram (mg) once daily.

| **Number of subjects in period 1** | Placebo | Empagliflozin 10 mg |
|---|---|---|
| Started | 3305 | 3304 |
| Treated | 3305 | 3304 |
| Completed | 2457 | 2549 |
| Not completed | 848 | 755 |
| Adverse event, serious fatal | 130 | 121 |
| Participant concerned about study treatment | 23 | 28 |
| Adverse event, non-fatal | 119 | 116 |
| Cannot attend clinic because of personal problems | 8 | 16 |
| Contraindicated drug started | 32 | 18 |
| Cannot attend clinic due to moving out of the area | 15 | 9 |
| Study drug stopped, reason missing | 336 | 294 |
| Doctor advice | 38 | 40 |
| Other (any category with <20 patients in total) | 58 | 45 |
| Participants' wish | 89 | 68 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Placebo |
| Reporting group description: | |
| Patients with evidence of chronic kidney disease (CKD) at risk of kidney disease progression, with or without diagnosed diabetes mellitus administered orally once daily film-coated tablets of placebo to match empagliflozin. | |
| Reporting group title | Empagliflozin 10 mg |
| Reporting group description: | |
| Patients with evidence of chronic kidney disease (CKD) at risk of kidney disease progression, with or without diagnosed diabetes mellitus administered orally once daily 10 milligram (mg) film-coated tablets of empagliflozin. | |

| Reporting group values | Placebo | Empagliflozin 10 mg | Total |
|---|---|---|---|
| Number of subjects | 3305 | 3304 | 6609 |
| Age categorical | | | |
| Randomised set (RS) included all randomised participants, whether treated or not. | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 1502 | 1501 | 3003 |
| From 65-84 years | 1744 | 1729 | 3473 |
| 85 years and over | 59 | 74 | 133 |
| Age Continuous | | | |
| Randomised set (RS) included all randomised participants, whether treated or not. | | | |
| Units: years | | | |
| arithmetic mean | 63.3 | 63.4 | |
| standard deviation | ± 13.9 | ± 13.9 | - |
| Sex: Female, Male | | | |
| Randomised set (RS) included all randomised participants, whether treated or not. | | | |
| Units: Participants | | | |
| Female | 1095 | 1097 | 2192 |
| Male | 2210 | 2207 | 4417 |
| Ethnicity (NIH/OMB) | | | |
| Randomised set (RS) included all randomised participants, whether treated or not. | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 119 | 103 | 222 |
| Not Hispanic or Latino | 723 | 708 | 1431 |
| Unknown or Not Reported | 2463 | 2493 | 4956 |
| Race/Ethnicity, Customized | | | |
| Randomised set (RS) included all randomised participants, whether treated or not. | | | |
| Units: Subjects | | | |
| White | 1920 | 1939 | 3859 |
| Black/ African-American | 134 | 128 | 262 |

| | | | |
|---|---|---|---|
| Asian | 1199 | 1194 | 2393 |
| Other including mixed race | 52 | 43 | 95 |

## End points

### End points reporting groups

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

Reporting group description:

Patients with evidence of chronic kidney disease (CKD) at risk of kidney disease progression, with or without diagnosed diabetes mellitus administered orally once daily film-coated tablets of placebo to match empagliflozin.

| Reporting group title | Empagliflozin 10 mg |
|---|---|

Reporting group description:

Patients with evidence of chronic kidney disease (CKD) at risk of kidney disease progression, with or without diagnosed diabetes mellitus administered orally once daily 10 milligram (mg) film-coated tablets of empagliflozin.

### Primary: Interventional part: Time to first occurrence of kidney disease progression or cardiovascular death ('as adjudicated')

| End point title | Interventional part: Time to first occurrence of kidney disease progression or cardiovascular death ('as adjudicated') |
|---|---|

End point description:

Incidence rate of first occurrence of kidney disease progression (KDP) or adjudicated cardiovascular death is reported in the Outcome Measure Data Table. Metrics such as the median time-to-event (TTE) was not estimable due to insufficient events being experienced.
Incidence rate= (Number of patients who experienced the event of first occurrence of KDP or cardiovascular death)*100/(patient years at risk (pt-yrs at risk). pt-yrs at risk= sum of time at risk [days] over all patients in a treatment group / 365.25.
Kidney disease progression was defined as:
- end stage kidney disease (defined as the initiation of maintenance dialysis or receipt of a kidney transplant)
OR
- a sustained decline in estimated glomerular filtration rate (eGFR) to <10 mL/min/1.73m^2
OR
- renal death
OR
- a sustained decline of ≥40% in eGFR from randomisation.

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

End point timeframe:

Follow-up period: From the day of randomisation to the day of the final follow-up visit, up to 1136 days.

| End point values | Placebo | Empagliflozin 10 mg | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 3305[1] | 3304[2] | | |
| Units: patients with events/100 pt-yrs at risk | | | | |
| number (confidence interval 95%) | 8.96 (8.23 to 9.72) | 6.85 (6.22 to 7.51) | | |

Notes:

[1] - Randomised set (RS) included all randomised participants, whether treated or not.

[2] - Randomised set (RS) included all randomised participants, whether treated or not.

### Statistical analyses

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

Statistical analysis description:

Hazard ratio (HR) of the time to first occurrence of kidney disease progression or CV death. HR is based on a Cox regression model with terms for age, sex, screening diabetes status, local screening estimated glomerular filtration rate Chronic Kidney Disease Epidemiology Collaboration (eGFR (CKD−EPI)), local screening Urine albumin-to-creatinine ratio (UACR), region and treatment.

Comparison vs. Placebo

| Comparison groups | Placebo v Empagliflozin 10 mg |
|---|---|
| Number of subjects included in analysis | 6609 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[3] |
| P-value | < 0.0001 |
| Method | Regression, Cox |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.72 |
| Confidence interval | |
| level | Other: 99.83 % |
| sides | 2-sided |
| lower limit | 0.59 |
| upper limit | 0.89 |

Notes:

[3] - Null hypothesis: There is no difference between the effect of placebo and the effect of empagliflozin.
Two-sided significance level of <0.0017 required at interim analysis.

## Secondary: Key secondary endpoint: Interventional part - Time to first hospitalization for heart failure (‘as adjudicated’) or cardiovascular death (‘as adjudicated’)

| End point title | Key secondary endpoint: Interventional part - Time to first hospitalization for heart failure (‘as adjudicated’) or cardiovascular death (‘as adjudicated’) |
|---|---|

End point description:

Incidence rate of first hospitalization for heart failure or cardiovascular death is reported in the Outcome Measure Data Table because metrics such as the median time-to-event (TTE) not estimable due to insufficient events being experienced.
Incidence rate= (Number of patients who experienced the event of first hospitalization for heart failure or cardiovascular death) *100/(patient years at risk (pt-yrs at risk)).
pt-yrs at risk= sum of time at risk [days] over all patients in a treatment group / 365.25.

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

End point timeframe:

Follow-up period: From the day of randomisation to the day of the final follow-up visit, up to 1140 days.

| End point values | Placebo | Empagliflozin 10 mg | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 3305[4] | 3304[5] | | |
| Units: patients with events/100 pt-yrs at risk | | | | |
| number (confidence interval 95%) | 2.39 (2.03 to 2.78) | 2.04 (1.70 to 2.40) | | |

Notes:

[4] - Randomised set (RS) included all randomised participants, whether treated or not.

[5] - Randomised set (RS) included all randomised participants, whether treated or not.

## Statistical analyses

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

Statistical analysis description:

Hazard ratio (HR) of the time to first hospitalization for heart failure or cardiovascular death. HR is based on a Cox regression model with terms for age, sex, screening diabetes status, local screening estimated glomerular filtration rate Chronic Kidney Disease Epidemiology Collaboration (eGFR (CKD−EPI)), local screening Urine albumin-to-creatinine ratio (UACR), region and treatment.

Comparison vs. Placebo

| Comparison groups | Placebo v Empagliflozin 10 mg |
|---|---|
| Number of subjects included in analysis | 6609 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[6] |
| P-value | = 0.1363 |
| Method | Regression, Cox |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.84 |
| Confidence interval | |
| level | Other: 98.55 % |
| sides | 2-sided |
| lower limit | 0.63 |
| upper limit | 1.12 |

Notes:

[6] - Null hypothesis: There is no difference between the effect of placebo and the effect of empagliflozin.
Two-sided significance level of <0.0145 required at interim analysis.

## Secondary: Key secondary endpoint: Interventional part - Time to occurrences of all-cause hospitalizations (first and recurrent combined)

| End point title | Key secondary endpoint: Interventional part - Time to occurrences of all-cause hospitalizations (first and recurrent combined) |
|---|---|

End point description:

Total number of all-cause hospitalizations (first and recurrent combined) is reported in the Outcome Measure Data Table. Conventional time-to-event (TTE) metrics such as the median not calculable for a recurrent TTE analysis.

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

End point timeframe:

Follow-up period: From the day of randomisation to the day of the final follow-up visit, up to 1140 days.

| End point values | Placebo | Empagliflozin 10 mg | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 3305[7] | 3304[8] | | |
| Units: events (first and recurrent) | 1895 | 1612 | | |

Notes:

[7] - Randomised set (RS) included all randomised participants, whether treated or not.

[8] - Randomised set (RS) included all randomised participants, whether treated or not.

## Statistical analyses

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

Statistical analysis description:

Hazard ratio (HR) of the time to occurrences of all-cause hospitalizations (first and recurrent combined). HR based on an analysis of recurrent events accounting for terminal events using a joint frailty model with terms for age, log(local screening UACR), local screening Chronic Kidney Disease Epidemiology Collaboration (eGFR (CKD−EPI)), treatment, sex, screening diabetes status, region.

Comparison vs. Placebo

| Comparison groups | Placebo v Empagliflozin 10 mg |
|---|---|
| Number of subjects included in analysis | 6609 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[9] |
| P-value | = 0.0022 |
| Method | Joint frailty model |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.86 |
| Confidence interval | |
| level | Other: 99.03 % |
| sides | 2-sided |
| lower limit | 0.76 |
| upper limit | 0.98 |

Notes:

[9] - Null hypothesis: There is no difference between the effect of placebo and the effect of empagliflozin. Two-sided significance level of <0.0097 required at interim analysis.

## Secondary: Key secondary endpoint: Interventional part - Time to death from any cause (‘as adjudicated’)

| End point title | Key secondary endpoint: Interventional part - Time to death from any cause (‘as adjudicated’) |
|---|---|

End point description:

Incidence rate of death from any cause is reported in the Outcome Measure Data Table. Metrics such as the median time-to-event (TTE) not estimable due to insufficient events being experienced.
Incidence rate of death from any cause = (Number of patients who experienced the event of death from any cause) * 100/(patient years at risk (pt-yrs at risk)). pt-yrs at risk= sum of time at risk [days] over all patients in a treatment group / 365.25.

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

End point timeframe:

Follow-up period: From the day of randomisation to the day of the final follow-up visit, up to 1140 days.

| End point values | Placebo | Empagliflozin 10 mg | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 3305[10] | 3304[11] | | |
| Units: patients with events/100 pt-yrs at risk | | | | |
| number (confidence interval 95%) | 2.59 (2.21 to 3.00) | 2.29 (1.94 to 2.68) | | |

Notes:

[10] - Randomised set (RS) included all randomised participants, whether treated or not.

[11] - Randomised set (RS) included all randomised participants, whether treated or not.

## Statistical analyses

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

Statistical analysis description:

Hazard ratio (HR) of the time to death from any cause. HR is based on a Cox regression model with terms for age, sex, screening diabetes status, local screening estimated glomerular filtration rate Chronic Kidney Disease Epidemiology Collaboration (eGFR (CKD−EPI)), local screening Urine albumin-to-creatinine ratio (UACR), region and treatment.

Comparison vs. Placebo

| Comparison groups | Placebo v Empagliflozin 10 mg |
|---|---|
| Number of subjects included in analysis | 6609 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[12] |
| P-value | = 0.2122 |
| Method | Regression, Cox |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.87 |
| Confidence interval | |
| level | Other: 97.1 % |
| sides | 2-sided |
| lower limit | 0.68 |
| upper limit | 1.11 |

Notes:

[12] - Null hypothesis: There is no difference between the effect of placebo and the effect of empagliflozin.
Two-sided significance level of <0.0290 required at interim analysis.

## Secondary: Interventional part: Time to first occurrence of kidney disease progression

| End point title | Interventional part: Time to first occurrence of kidney disease progression |
|---|---|

End point description:

Incidence rate of first occurrence of kidney disease progression is reported in the Outcome Measure Data Table. Metrics such as the median time-to-event (TTE) not estimable due to insufficient events being experienced.
Incidence rate of first occurrence of kidney disease progression= (Number of patients who experienced the event of first occurrence of kidney disease progression) *100/(patient years at risk (pt-yrs at risk)).
pt-yrs at risk= sum of time at risk [days] over all patients in a treatment group / 365.25.
Kidney disease progression was defined as:
- end stage kidney disease (defined as the initiation of maintenance dialysis or receipt of a kidney transplant)
OR
- a sustained decline in estimated glomerular filtration rate (eGFR) to <10 mL/min/1.73m^2
OR
- renal death
OR
- a sustained decline of ≥40% in eGFR from randomisation).

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

End point timeframe:

Follow-up period: From the day of randomisation to the day of the final follow-up visit, up to 1136 days.

| **End point values** | Placebo | Empagliflozin 10 mg | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 3305[13] | 3304[14] | | |
| Units: patients with events/100 pt-yrs at risk | | | | |
| number (confidence interval 95%) | 8.09 (7.40 to 8.81) | 6.09 (5.50 to 6.72) | | |

Notes:

[13] - Randomised set (RS) included all randomised participants, whether treated or not.

[14] - Randomised set (RS) included all randomised participants, whether treated or not.

### Statistical analyses

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

Statistical analysis description:

Hazard ratio (HR) of the time to first occurrence of kidney disease progression. HR is based on a Cox regression model with terms for age, sex, screening diabetes status, local screening estimated glomerular filtration rate Chronic Kidney Disease Epidemiology Collaboration (eGFR (CKD−EPI)), local screening urine albumin-to-creatinine ratio (UACR), region and treatment.

Comparison vs. Placebo

| Comparison groups | Placebo v Empagliflozin 10 mg |
|---|---|
| Number of subjects included in analysis | 6609 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[15] |
| P-value | < 0.0001 |
| Method | Regression, Cox |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.71 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.62 |
| upper limit | 0.81 |

Notes:

[15] - Null hypothesis: There is no difference between the effect of placebo and the effect of empagliflozin.

### Secondary: Interventional part: Time to first occurrence cardiovascular death ('as adjudicated') or end stage kidney disease (ESKD)

| End point title | Interventional part: Time to first occurrence cardiovascular death ('as adjudicated') or end stage kidney disease (ESKD) |
|---|---|

End point description:

Incidence rate of first occurrence of cardiovascular death or end stage kidney disease (ESKD) is reported in the Outcome Measure Data Table. Metrics such as the median time-to-event (TTE) not estimable due to insufficient events being experienced.
Incidence rate of first occurrence cardiovascular death or end stage kidney disease (ESKD)= (Number of patients who experienced the event of first occurrence of cardiovascular death or end stage kidney disease (ESKD)) *100/(patient years at risk (pt-yrs at risk)). pt-yrs at risk= sum of time at risk [days]

over all patients in a treatment group / 365.25.
ESKD was defined as the initiation of maintenance dialysis or receipt of a kidney transplant.

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

End point timeframe:

Follow-up period: From the day of randomisation to the day of the final follow-up visit, up to 1140 days.

| **End point values** | Placebo | Empagliflozin 10 mg | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 3305[16] | 3304[17] | | |
| Units: patients with events/100 pt-yrs at risk | | | | |
| number (confidence interval 95%) | 3.45 (3.01 to 3.92) | 2.55 (2.18 to 2.96) | | |

Notes:

[16] - Randomised set (RS) included all randomised participants, whether treated or not.

[17] - Randomised set (RS) included all randomised participants, whether treated or not.

## Statistical analyses

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

Statistical analysis description:

Hazard ratio (HR) of the time to first occurrence cardiovascular death or end stage kidney disease (ESKD). HR is based on a Cox regression model with terms for age, sex, screening diabetes status, local screening estimated glomerular filtration rate Chronic Kidney Disease Epidemiology Collaboration (eGFR (CKD−EPI)), local screening urine albumin-to-creatinine ratio (UACR), region and treatment.

Comparison vs. Placebo

| Comparison groups | Placebo v Empagliflozin 10 mg |
|---|---|
| Number of subjects included in analysis | 6609 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[18] |
| P-value | = 0.0017 |
| Method | Regression, Cox |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.72 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.59 |
| upper limit | 0.89 |

Notes:

[18] - Null hypothesis: There is no difference between the effect of placebo and the effect of empagliflozin.

## Secondary: Interventional part: Time to cardiovascular death (‘as adjudicated’)

| End point title | Interventional part: Time to cardiovascular death (‘as adjudicated’) |
|---|---|

End point description:

Incidence rate of first occurrence of kidney disease progression is reported in the Outcome Measure Data Table. Metrics such as the median time-to-event (TTE) not estimable due to insufficient events being experienced.
Incidence rate of cardiovascular death is reported in the Outcome Measure Data Table. Metrics such as the median time-to-event (TTE) not estimable due to too few events being experienced.

Incidence rate of cardiovascular death= (Number of patients who experienced the event of cardiovascular death) *100/(patient years at risk (pt-yrs at risk)). pt-yrs at risk= sum of time at risk [days] over all patients in a treatment group / 365.25.

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

End point timeframe:

Follow-up period: From the day of randomisation to the day of the final follow-up visit, up to 1140 days.

| **End point values** | Placebo | Empagliflozin 10 mg | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 3305[19] | 3304[20] | | |
| Units: patients with events/100 pt-yrs at risk | | | | |
| number (confidence interval 95%) | 1.08 (0.84 to 1.35) | 0.91 (0.69 to 1.15) | | |

Notes:

[19] - Randomised set (RS) included all randomised participants, whether treated or not.

[20] - Randomised set (RS) included all randomised participants, whether treated or not.

## Statistical analyses

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

Statistical analysis description:

Hazard ratio (HR) of the time to cardiovascular death. HR is based on a Cox regression model with terms for age, sex, screening diabetes status, local screening estimated glomerular filtration rate Chronic Kidney Disease Epidemiology Collaboration (eGFR (CKD−EPI)), local screening urine albumin-to-creatinine ratio (UACR), region and treatment.

Comparison vs. Placebo

| Comparison groups | Placebo v Empagliflozin 10 mg |
|---|---|
| Number of subjects included in analysis | 6609 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[21] |
| P-value | = 0.2932 |
| Method | Regression, Cox |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.83 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.59 |
| upper limit | 1.17 |

Notes:

[21] - Null hypothesis: There is no difference between the effect of placebo and the effect of empagliflozin.

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

[All-cause Mortality]: From randomisation until end of study, up to 1171 days.
[Serious adverse events (AE) and other AE]: From randomisation until 7 days (Residual Effect Period) after the last drug intake, up to 1147 days.

Adverse event reporting additional description:

Treated Set (TS): This patient set included all patients who were dispensed randomised study medication.
Only protocol pre-specified non-serious Adverse Events (AEs) were collected.

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| Assessment type | Systematic |

### Dictionary used

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| Dictionary name | MedDRA |
| Dictionary version | 20.1 |

### Reporting groups

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| Reporting group title | Empa 10mg |

Reporting group description:

Patients with evidence of chronic kidney disease (CKD) at risk of kidney disease progression, with or without diagnosed diabetes mellitus administered orally once daily 10 milligram (mg) film-coated tablets of empagliflozin.

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| Reporting group title | Placebo |

Reporting group description:

Patients with evidence of chronic kidney disease (CKD) at risk of kidney disease progression, with or without diagnosed diabetes mellitus administered orally once daily film-coated tablets of placebo to match empagliflozin.

| Serious adverse events | Empa 10mg | Placebo | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1089 / 3304 (32.96%) | 1167 / 3305 (35.31%) | |
| number of deaths (all causes) | 159 | 182 | |
| number of deaths resulting from adverse events | 130 | 137 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Acute myeloid leukaemia | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Adenocarcinoma | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Adenocarcinoma pancreas | | | |

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|---|---|---|---|
| subjects affected / exposed | 2 / 3304 (0.06%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Adenosquamous cell lung cancer | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Adenosquamous cell lung cancer stage IV | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anal cancer | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anaplastic astrocytoma | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Angiosarcoma | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Basal cell carcinoma | | | |
| subjects affected / exposed | 11 / 3304 (0.33%) | 6 / 3305 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 11 | 0 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Benign breast neoplasm | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Benign gastrointestinal neoplasm | | | |

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|---|---|---|---|
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Benign lung neoplasm | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Benign neoplasm of skin | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bile duct cancer | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Biliary neoplasm | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bladder adenocarcinoma stage III | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bladder cancer | | | |
| subjects affected / exposed | 6 / 3304 (0.18%) | 4 / 3305 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bladder transitional cell carcinoma | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bowen's disease | | | |

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|---|---|---|---|
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Brain neoplasm | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Breast cancer | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Breast cancer female | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 3 / 3305 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Breast cancer in situ | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Breast cancer male | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Breast cancer metastatic | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Breast cancer stage II | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchial carcinoma | | | |

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|---|---|---|---|
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Carcinoid tumour of the prostate | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Carcinoma in situ of penis | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Carcinoma in situ of skin | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chronic lymphocytic leukaemia | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chronic myeloid leukaemia | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Clear cell sarcoma of the kidney | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colon cancer | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 4 / 3305 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colon cancer metastatic | | | |

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|---|---|---|---|
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Colon cancer stage 0 | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colon cancer stage I | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colon cancer stage III | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colon cancer stage IV | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Colorectal cancer | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colorectal cancer stage III | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ear neoplasm malignant | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Enchondromatosis | | | |

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|---|---|---|---|---|
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | | |
| Endometrial cancer | | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 0 / 3305 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | | |
| Extranodal marginal zone B-cell lymphoma (MALT type) | | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | | |
| Follicle centre lymphoma, follicular grade I, II, III | | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | | |
| Gallbladder cancer | | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | | |
| Gallbladder cancer metastatic | | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 0 / 3305 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | | |
| Gastric cancer | | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | | |
| Gastric cancer recurrent | | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | | |
| Gastrooesophageal cancer | | | | |

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|---|---|---|---|
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatic cancer | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 6 / 3305 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 7 | |
| deaths causally related to treatment / all | 0 / 2 | 0 / 1 | |
| Hepatic cancer stage II | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypopharyngeal cancer | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intestinal adenocarcinoma | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Invasive breast carcinoma | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lipoma | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lung adenocarcinoma | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Lung cancer metastatic | | | |

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|---|---|---|---|
| subjects affected / exposed | 1 / 3304 (0.03%) | 5 / 3305 (0.15%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 6 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 4 | |
| Lung neoplasm malignant | | | |
| subjects affected / exposed | 3 / 3304 (0.09%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Malignant melanoma | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Malignant melanoma in situ | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Malignant neoplasm of renal pelvis | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Melanoma recurrent | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metastases to liver | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metastases to lung | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metastases to lymph nodes | | | |

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|---|---|---|---|
| subjects affected / exposed | 1 / 3304 (0.03%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metastases to spinal cord | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metastatic bronchial carcinoma | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Metastatic malignant melanoma | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Metastatic renal cell carcinoma | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Monoclonal gammopathy | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myelodysplastic syndrome | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myeloproliferative neoplasm | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neuroendocrine tumour | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Non-Hodgkin's lymphoma | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Non-small cell lung cancer | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Non-small cell lung cancer stage I | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Non-small cell lung cancer stage II | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Non-small cell lung cancer stage IV | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Oropharyngeal cancer | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Osteosarcoma | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ovarian cancer metastatic | | | |

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|---|---|---|---|
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Ovarian neoplasm | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancreatic carcinoma | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 2 | |
| Pancreatic carcinoma metastatic | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 3 / 3305 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 2 | 0 / 2 | |
| Pancreatic carcinoma stage II | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancreatic carcinoma stage IV | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Peritoneal sarcoma | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Plasma cell myeloma | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Plasma cell myeloma recurrent | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Plasmacytoma | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pleural neoplasm | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Prostate cancer | | | |
| subjects affected / exposed | 8 / 3304 (0.24%) | 10 / 3305 (0.30%) | |
| occurrences causally related to treatment / all | 0 / 8 | 0 / 10 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Prostate cancer metastatic | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Prostate cancer recurrent | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rectal cancer | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rectosigmoid cancer | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal cancer | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 3304 (0.06%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal cancer metastatic | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal cancer recurrent | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal cancer stage II | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal cell carcinoma | | | |
| subjects affected / exposed | 6 / 3304 (0.18%) | 4 / 3305 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 6 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Renal neoplasm | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin cancer | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 3 / 3305 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Small cell lung cancer | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Small cell lung cancer metastatic | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | |
| Soft tissue neoplasm | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal cord neoplasm | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Squamous cell carcinoma | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Squamous cell carcinoma of lung | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Squamous cell carcinoma of skin | | | |
| subjects affected / exposed | 3 / 3304 (0.09%) | 3 / 3305 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thymoma malignant | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Thyroid adenoma | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thyroid cancer | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tongue neoplasm malignant stage unspecified | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Transformation to acute myeloid leukaemia | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Uterine leiomyoma | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metastatic gastric cancer | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| **Vascular disorders** | | | |
| Arterial stenosis | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Arterial occlusive disease | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Aortic occlusion | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Aortic dissection rupture | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Aortic dissection | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Aortic aneurysm rupture | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Aortic aneurysm | | | |
| subjects affected / exposed | 3 / 3304 (0.09%) | 3 / 3305 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood pressure inadequately controlled | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypertensive crisis | | | |
| subjects affected / exposed | 5 / 3304 (0.15%) | 8 / 3305 (0.24%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 8 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypertension | | | |
| subjects affected / exposed | 3 / 3304 (0.09%) | 8 / 3305 (0.24%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 9 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haematoma | | | |
| subjects affected / exposed | 3 / 3304 (0.09%) | 3 / 3305 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Deep vein thrombosis | | | |

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|---|---|---|---|
| subjects affected / exposed | 4 / 3304 (0.12%) | 9 / 3305 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 9 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Circulatory collapse | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| CT hypotension complex | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypertensive emergency | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypovolaemic shock | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Temporal arteritis | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Malignant hypertension | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Necrosis ischaemic | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Orthostatic hypotension | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 3304 (0.00%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pelvic venous thrombosis | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peripheral arterial occlusive disease | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peripheral artery occlusion | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peripheral artery stenosis | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peripheral artery thrombosis | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peripheral ischaemia | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peripheral vascular disorder | | | |
| subjects affected / exposed | 4 / 3304 (0.12%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vein rupture | | | |

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|---|---|---|---|
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vasculitis | | | |
| subjects affected / exposed | 4 / 3304 (0.12%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 2 / 4 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thrombosis | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Surgical and medical procedures | | | |
| Aneurysm repair | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Angioplasty | | | |
| subjects affected / exposed | 3 / 3304 (0.09%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ankle operation | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Aortic aneurysm repair | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 4 / 3305 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Aortic valve repair | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Aortic valve replacement | | | |

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|---|---|---|---|
| subjects affected / exposed | 3 / 3304 (0.09%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Appendicectomy | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 3 / 3305 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Arterial bypass operation | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Arterial repair | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Arterial stent insertion | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Arteriovenous fistula operation | | | |
| subjects affected / exposed | 4 / 3304 (0.12%) | 8 / 3305 (0.24%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 9 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Arteriovenous shunt operation | | | |
| subjects affected / exposed | 8 / 3304 (0.24%) | 12 / 3305 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 8 | 0 / 13 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bladder catheter removal | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bladder catheterisation | | | |

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|---|---|---|---|
| subjects affected / exposed | 2 / 3304 (0.06%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bladder lesion excision | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bladder operation | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bladder polypectomy | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bone debridement | | | |
| subjects affected / exposed | 3 / 3304 (0.09%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bone operation | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| CSF shunt operation | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac ablation | | | |
| subjects affected / exposed | 5 / 3304 (0.15%) | 4 / 3305 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac operation | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 3304 (0.00%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac pacemaker battery replacement | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac pacemaker insertion | | | |
| subjects affected / exposed | 10 / 3304 (0.30%) | 12 / 3305 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 10 | 0 / 12 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac pacemaker removal | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac pacemaker replacement | | | |
| subjects affected / exposed | 4 / 3304 (0.12%) | 3 / 3305 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac resynchronisation therapy | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardioversion | | | |
| subjects affected / exposed | 3 / 3304 (0.09%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Carotid artery stent insertion | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Carotid endarterectomy | | | |

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|---|---|---|---|
| subjects affected / exposed | 3 / 3304 (0.09%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cataract operation | | | |
| subjects affected / exposed | 12 / 3304 (0.36%) | 27 / 3305 (0.82%) | |
| occurrences causally related to treatment / all | 0 / 16 | 0 / 43 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chemotherapy | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chest wall operation | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholecystectomy | | | |
| subjects affected / exposed | 5 / 3304 (0.15%) | 7 / 3305 (0.21%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 7 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colectomy | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colostomy | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colostomy closure | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Coronary angioplasty | | | |

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|---|---|---|---|
| subjects affected / exposed | 1 / 3304 (0.03%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Coronary arterial stent insertion | | | |
| subjects affected / exposed | 5 / 3304 (0.15%) | 3 / 3305 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Coronary artery bypass | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 8 / 3305 (0.24%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 8 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cyst removal | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dialysis device insertion | | | |
| subjects affected / exposed | 11 / 3304 (0.33%) | 19 / 3305 (0.57%) | |
| occurrences causally related to treatment / all | 0 / 11 | 0 / 19 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ear operation | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Elbow operation | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Endarterectomy | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Endometrial ablation | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| External fixation of fracture | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Eye operation | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Eyelid operation | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Foot amputation | | | |
| subjects affected / exposed | 5 / 3304 (0.15%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fracture treatment | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gallbladder operation | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastric operation | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastric stapling | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal surgery | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Glaucoma surgery | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemorrhoid operation | | | |
| subjects affected / exposed | 4 / 3304 (0.12%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Heart valve replacement | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatectomy | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatic embolisation | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hernia repair | | | |
| subjects affected / exposed | 4 / 3304 (0.12%) | 5 / 3305 (0.15%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hip arthroplasty | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 3 / 3304 (0.09%) | 4 / 3305 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hip surgery | | | |
| subjects affected / exposed | 6 / 3304 (0.18%) | 6 / 3305 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hospitalisation | | | |
| subjects affected / exposed | 10 / 3304 (0.30%) | 13 / 3305 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 12 | 0 / 18 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hysterectomy | | | |
| subjects affected / exposed | 3 / 3304 (0.09%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Implantable defibrillator insertion | | | |
| subjects affected / exposed | 3 / 3304 (0.09%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Implantable defibrillator replacement | | | |
| subjects affected / exposed | 3 / 3304 (0.09%) | 3 / 3305 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intervertebral disc operation | | | |
| subjects affected / exposed | 4 / 3304 (0.12%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intestinal polypectomy | | | |
| subjects affected / exposed | 5 / 3304 (0.15%) | 6 / 3305 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intra-cerebral aneurysm operation | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Joint arthroplasty | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 3 / 3305 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Joint surgery | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Knee arthroplasty | | | |
| subjects affected / exposed | 9 / 3304 (0.27%) | 4 / 3305 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 9 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Knee operation | | | |
| subjects affected / exposed | 6 / 3304 (0.18%) | 10 / 3305 (0.30%) | |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 10 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Large intestine operation | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Leg amputation | | | |
| subjects affected / exposed | 7 / 3304 (0.21%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 7 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Liver operation | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Low density lipoprotein apheresis | | | |

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|---|---|---|---|
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lung operation | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mastectomy | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 3 / 3305 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Meniscus operation | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 3 / 3305 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Middle ear operation | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mitral valve repair | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nasal operation | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nephrectomy | | | |
| subjects affected / exposed | 3 / 3304 (0.09%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oesophageal operation | | | |

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|---|---|---|---|
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oophorectomy | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Open reduction of fracture | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oral surgery | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ovarian operation | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Packed red blood cell transfusion | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pain management | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancreatic operation | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Parathyroidectomy | | | |

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|---|---|---|---|
| subjects affected / exposed | 1 / 3304 (0.03%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pelvic floor repair | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Percutaneous coronary intervention | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 3 / 3305 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peripheral artery angioplasty | | | |
| subjects affected / exposed | 3 / 3304 (0.09%) | 7 / 3305 (0.21%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 8 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peripheral artery bypass | | | |
| subjects affected / exposed | 3 / 3304 (0.09%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peripheral artery stent insertion | | | |
| subjects affected / exposed | 5 / 3304 (0.15%) | 4 / 3305 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peripheral endarterectomy | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peripheral revascularisation | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Prostatic operation | | | |

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|---|---|---|---|
| subjects affected / exposed | 2 / 3304 (0.06%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Radical prostatectomy | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Radiotherapy | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 3 / 3305 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rectal prolapse repair | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Removal of foreign body from joint | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Removal of internal fixation | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal stone removal | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Retinal laser coagulation | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Retinal operation | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Shoulder operation | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 5 / 3305 (0.15%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin graft | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal cord operation | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal fusion surgery | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal laminectomy | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal operation | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 5 / 3305 (0.15%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 7 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Stem cell transplant | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Subdural haematoma evacuation | | | |

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|---|---|---|---|
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Transurethral prostatectomy | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Transurethral bladder resection | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Transmyocardial revascularisation | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tracheostomy | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tooth extraction | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tongue operation | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ureteral stent removal | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thyroidectomy | | | |

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|---|---|---|---|
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thyroid operation | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thrombectomy | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thoracic operation | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tricuspid valve repair | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ureteral stent insertion | | | |
| subjects affected / exposed | 3 / 3304 (0.09%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Toe amputation | | | |
| subjects affected / exposed | 16 / 3304 (0.48%) | 11 / 3305 (0.33%) | |
| occurrences causally related to treatment / all | 0 / 17 | 0 / 13 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Uterine operation | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Uterine dilation and curettage | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ureteric operation | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ureteric calculus removal | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pregnancy, puerperium and perinatal conditions | | | |
| Abortion | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Death | | | |
| subjects affected / exposed | 10 / 3304 (0.30%) | 10 / 3305 (0.30%) | |
| occurrences causally related to treatment / all | 0 / 10 | 0 / 10 | |
| deaths causally related to treatment / all | 0 / 10 | 0 / 10 | |
| Autoresuscitation | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chest discomfort | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chest pain | | | |
| subjects affected / exposed | 7 / 3304 (0.21%) | 12 / 3305 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 7 | 0 / 12 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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|---|---|---|---|
| Sudden cardiac death | | | |
| subjects affected / exposed | 12 / 3304 (0.36%) | 17 / 3305 (0.51%) | |
| occurrences causally related to treatment / all | 0 / 12 | 0 / 17 | |
| deaths causally related to treatment / all | 0 / 12 | 0 / 17 | |
| Pain | | | |
| subjects affected / exposed | 4 / 3304 (0.12%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oedema peripheral | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oedema | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 4 / 3305 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 4 / 3304 (0.12%) | 3 / 3305 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Necrosis | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Incarcerated hernia | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General physical health deterioration | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 3 / 3305 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gait disturbance | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3304 (0.00%) | 3 / 3305 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sudden death | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Vascular stent thrombosis | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular stent occlusion | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Immune system disorders | | | |
| Graft versus host disease in gastrointestinal tract | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anaphylactic reaction | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Allergy to vaccine | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Social circumstances | | | |
| Social problem | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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|---|---|---|---|
| Reproductive system and breast disorders | | | |
| Benign prostatic hyperplasia | | | |
| subjects affected / exposed | 3 / 3304 (0.09%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dysfunctional uterine bleeding | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ovarian failure | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Uterine polyp | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute pulmonary oedema | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Acute respiratory failure | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 5 / 3305 (0.15%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Apnoea | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Aspiration | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3304 (0.00%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Asthma | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchiectasis | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 3 / 3304 (0.09%) | 4 / 3305 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Chronic respiratory failure | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Combined pulmonary fibrosis and emphysema | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dyspnoea | | | |
| subjects affected / exposed | 6 / 3304 (0.18%) | 5 / 3305 (0.15%) | |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Eosinophilic pneumonia | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Epistaxis | | | |

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|---|---|---|---|
| subjects affected / exposed | 1 / 3304 (0.03%) | 4 / 3305 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemoptysis | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemothorax | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Hypoxia | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Interstitial lung disease | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Laryngeal oedema | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pleural effusion | | | |
| subjects affected / exposed | 6 / 3304 (0.18%) | 3 / 3305 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pleurisy | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia aspiration | | | |

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|---|---|---|---|
| subjects affected / exposed | 1 / 3304 (0.03%) | 5 / 3305 (0.15%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Pneumonitis | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumothorax | | | |
| subjects affected / exposed | 3 / 3304 (0.09%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 4 / 3304 (0.12%) | 8 / 3305 (0.24%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 8 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary fibrosis | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 5 / 3305 (0.15%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Pulmonary hypertension | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 4 / 3305 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Pulmonary oedema | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary sarcoidosis | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory failure | | | |

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|---|---|---|---|
| subjects affected / exposed | 2 / 3304 (0.06%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Sleep apnoea syndrome | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vocal cord disorder | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| Acute psychosis | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Alcohol abuse | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anxiety | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bipolar disorder | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Confusional state | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 3 / 3305 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Delirium | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Depression | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mania | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychotic behaviour | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychotic disorder | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Suicide attempt | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Hepatic cirrhosis | | | |
| subjects affected / exposed | 3 / 3304 (0.09%) | 4 / 3305 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 7 | 0 / 6 | |
| deaths causally related to treatment / all | 0 / 2 | 0 / 0 | |
| Gallbladder polyp | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gallbladder necrosis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholelithiasis | | | |
| subjects affected / exposed | 6 / 3304 (0.18%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholecystitis | | | |
| subjects affected / exposed | 9 / 3304 (0.27%) | 6 / 3305 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 10 | 0 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholangitis | | | |
| subjects affected / exposed | 4 / 3304 (0.12%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Hepatic function abnormal | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatitis cholestatic | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatitis toxic | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 4 / 3305 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Jaundice | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Liver injury | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 5 / 3304 (0.15%) | 7 / 3305 (0.21%) | |
| occurrences causally related to treatment / all | 1 / 5 | 1 / 7 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | |
| Non-alcoholic fatty liver | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Non-alcoholic steatohepatitis | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Portal vein thrombosis | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatitis | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Angiogram | | | |
| subjects affected / exposed | 4 / 3304 (0.12%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Angiogram peripheral | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anticoagulation drug level above therapeutic | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Arteriogram carotid | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Arteriogram coronary | | | |
| subjects affected / exposed | 3 / 3304 (0.09%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Biopsy intestine | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Biopsy kidney | | | |
| subjects affected / exposed | 6 / 3304 (0.18%) | 3 / 3305 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Biopsy liver | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 3 / 3305 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Biopsy prostate | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood creatinine increased | | | |
| subjects affected / exposed | 43 / 3304 (1.30%) | 56 / 3305 (1.69%) | |
| occurrences causally related to treatment / all | 2 / 47 | 1 / 61 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood glucose increased | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3304 (0.00%) | 3 / 3305 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood magnesium decreased | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood potassium decreased | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 3 / 3305 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood potassium increased | | | |
| subjects affected / exposed | 76 / 3304 (2.30%) | 87 / 3305 (2.63%) | |
| occurrences causally related to treatment / all | 0 / 81 | 0 / 89 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood pressure decreased | | | |
| subjects affected / exposed | 4 / 3304 (0.12%) | 4 / 3305 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood pressure increased | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood sodium decreased | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchoscopy | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Catheterisation cardiac | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 8 / 3304 (0.24%) | 11 / 3305 (0.33%) | |
| occurrences causally related to treatment / all | 0 / 9 | 0 / 12 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colonoscopy | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 9 / 3305 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 9 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Computerised tomogram | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Coronavirus test positive | | | |
| subjects affected / exposed | 6 / 3304 (0.18%) | 3 / 3305 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cystoscopy | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Endoscopy gastrointestinal | | | |
| subjects affected / exposed | 3 / 3304 (0.09%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Endoscopy upper gastrointestinal tract | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Heart rate irregular | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Investigation | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 4 / 3304 (0.12%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Laryngoscopy | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nuclear magnetic resonance imaging abdominal | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sleep study | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ultrasound kidney | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ultrasound liver | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ultrasound scan | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ureteroscopy | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |

| | | | |
|---|---|---|---|
| Ankle fracture | | | |
| subjects affected / exposed | 6 / 3304 (0.18%) | 3 / 3305 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Animal bite | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Acetabulum fracture | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Accidental overdose | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Femur fracture | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 9 / 3305 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 9 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fibula fracture | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Foot fracture | | | |
| subjects affected / exposed | 5 / 3304 (0.15%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Forearm fracture | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Foreign body aspiration | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Fracture | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fractured ischium | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Coronary artery restenosis | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 3 / 3305 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Concussion | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Clavicle fracture | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac valve replacement complication | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Femoral neck fracture | | | |
| subjects affected / exposed | 3 / 3304 (0.09%) | 5 / 3305 (0.15%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Back injury | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fall | | | |
| subjects affected / exposed | 17 / 3304 (0.51%) | 19 / 3305 (0.57%) | |
| occurrences causally related to treatment / all | 0 / 18 | 0 / 22 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Facial bones fracture | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 3 / 3305 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Crush injury | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Burns second degree | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Fractured sacrum | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hand fracture | | | |
| subjects affected / exposed | 5 / 3304 (0.15%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Head injury | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hip fracture | | | |

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|---|---|---|---|
| subjects affected / exposed | 3 / 3304 (0.09%) | 7 / 3305 (0.21%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 7 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | |
| Humerus fracture | | | |
| subjects affected / exposed | 5 / 3304 (0.15%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Inadequate haemodialysis | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Incisional hernia | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Joint dislocation | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lumbar vertebral fracture | | | |
| subjects affected / exposed | 3 / 3304 (0.09%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Multiple fractures | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Muscle injury | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Muscle strain | | | |

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|---|---|---|---|
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oesophageal injury | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Patella fracture | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pelvic fracture | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peripheral artery restenosis | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumothorax traumatic | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Post angioplasty restenosis | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Post procedural haematoma | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Post procedural haemorrhage | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 3304 (0.06%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Post procedural myocardial infarction | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pubis fracture | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Radius fracture | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rib fracture | | | |
| subjects affected / exposed | 4 / 3304 (0.12%) | 5 / 3305 (0.15%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Road traffic accident | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Skin injury | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin wound | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Soft tissue injury | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 3304 (0.06%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal compression fracture | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal cord injury lumbar | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal fracture | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Splenic injury | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Stab wound | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sternal fracture | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Subdural haematoma | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 3 / 3305 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Subdural haemorrhage | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tendon injury | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tendon rupture | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thoracic vertebral fracture | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tibia fracture | | | |
| subjects affected / exposed | 3 / 3304 (0.09%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Traumatic intracranial haemorrhage | | | |
| subjects affected / exposed | 3 / 3304 (0.09%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Upper limb fracture | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary retention postoperative | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vaccination complication | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular graft thrombosis | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular injury | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular procedure complication | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Wound | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Wound dehiscence | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Wrist fracture | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Congenital, familial and genetic disorders | | | |
| Myocardial bridging | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Heart block congenital | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Congenital vesicoureteric reflux | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Adenomatous polyposis coli | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteoporosis-pseudoglioma syndrome | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Phimosis | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thalassaemia | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 6 / 3304 (0.18%) | 5 / 3305 (0.15%) | |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Acute coronary syndrome | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Angina pectoris | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 8 / 3304 (0.24%) | 19 / 3305 (0.57%) | |
| occurrences causally related to treatment / all | 0 / 8 | 0 / 19 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Angina unstable | | | |
| subjects affected / exposed | 11 / 3304 (0.33%) | 9 / 3305 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 12 | 0 / 11 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Aortic valve disease | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 2 | |
| Aortic valve incompetence | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Aortic valve stenosis | | | |
| subjects affected / exposed | 4 / 3304 (0.12%) | 7 / 3305 (0.21%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 7 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Arrhythmia | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 18 / 3304 (0.54%) | 32 / 3305 (0.97%) | |
| occurrences causally related to treatment / all | 0 / 20 | 0 / 35 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac arrest | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrioventricular block | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 3 / 3304 (0.09%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrioventricular block complete | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrioventricular block second degree | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Bradyarrhythmia | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bradycardia | | | |
| subjects affected / exposed | 5 / 3304 (0.15%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bundle branch block | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrial flutter | | | |
| subjects affected / exposed | 4 / 3304 (0.12%) | 4 / 3305 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 7 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac failure | | | |
| subjects affected / exposed | 41 / 3304 (1.24%) | 44 / 3305 (1.33%) | |
| occurrences causally related to treatment / all | 0 / 53 | 0 / 59 | |
| deaths causally related to treatment / all | 0 / 9 | 0 / 10 | |
| Sinus arrest | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulseless electrical activity | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pericarditis | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pericardial effusion | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Palpitations | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 4 / 3305 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myocarditis | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myocardial infarction | | | |
| subjects affected / exposed | 39 / 3304 (1.18%) | 31 / 3305 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 41 | 0 / 34 | |
| deaths causally related to treatment / all | 0 / 4 | 0 / 4 | |
| Mitral valve incompetence | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 3 / 3305 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Malignant hypertensive heart disease | | | |

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|---|---|---|---|
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ischaemic cardiomyopathy | | | |
| subjects affected / exposed | 33 / 3304 (1.00%) | 45 / 3305 (1.36%) | |
| occurrences causally related to treatment / all | 0 / 41 | 0 / 63 | |
| deaths causally related to treatment / all | 0 / 10 | 0 / 7 | |
| Hypertensive cardiomyopathy | | | |
| subjects affected / exposed | 5 / 3304 (0.15%) | 10 / 3305 (0.30%) | |
| occurrences causally related to treatment / all | 0 / 8 | 0 / 13 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Coronary vein stenosis | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac fibrillation | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac sarcoidosis | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Coronary artery disease | | | |
| subjects affected / exposed | 7 / 3304 (0.21%) | 14 / 3305 (0.42%) | |
| occurrences causally related to treatment / all | 0 / 7 | 0 / 16 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Coronary artery stenosis | | | |
| subjects affected / exposed | 3 / 3304 (0.09%) | 4 / 3305 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ventricular tachyarrhythmia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3304 (0.00%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ventricular fibrillation | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Ventricular extrasystoles | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ventricular arrhythmia | | | |
| subjects affected / exposed | 3 / 3304 (0.09%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Trifascicular block | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tachycardia | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sinus bradycardia | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 3 / 3305 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ventricular tachycardia | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Supraventricular tachycardia | | | |

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|---|---|---|---|
| subjects affected / exposed | 2 / 3304 (0.06%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Basal ganglia infarction | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Basilar artery thrombosis | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Brain stem infarction | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Carotid artery aneurysm | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Carotid artery stenosis | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebellar infarction | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebral infarction | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 3 / 3305 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebral ischaemia | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cranial nerve paralysis | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dementia | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dementia Alzheimer's type | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Diabetic neuropathy | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dizziness | | | |
| subjects affected / exposed | 3 / 3304 (0.09%) | 5 / 3305 (0.15%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dizziness postural | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Encephalopathy | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Epilepsy | | | |

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|---|---|---|---|
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemorrhagic stroke | | | |
| subjects affected / exposed | 10 / 3304 (0.30%) | 6 / 3305 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 10 | 0 / 6 | |
| deaths causally related to treatment / all | 0 / 3 | 0 / 4 | |
| Headache | | | |
| subjects affected / exposed | 6 / 3304 (0.18%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hemiplegia | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypoglycaemic coma | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypoglycaemic encephalopathy | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypoglycaemic unconsciousness | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intracranial aneurysm | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ischaemic stroke | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 30 / 3304 (0.91%) | 34 / 3305 (1.03%) | |
| occurrences causally related to treatment / all | 1 / 32 | 1 / 39 | |
| deaths causally related to treatment / all | 0 / 6 | 0 / 3 | |
| Lacunar infarction | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Loss of consciousness | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 3 / 3305 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Microvascular cranial nerve palsy | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Migraine | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Movement disorder | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neuropathy peripheral | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Paraesthesia | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Parkinson's disease | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 3304 (0.06%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peripheral sensorimotor neuropathy | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peripheral sensory neuropathy | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Polyneuropathy | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Post stroke seizure | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Presyncope | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 6 / 3305 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sciatica | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Seizure | | | |
| subjects affected / exposed | 4 / 3304 (0.12%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Speech disorder | | | |

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|---|---|---|---|
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal cord herniation | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Status epilepticus | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Syncope | | | |
| subjects affected / exposed | 16 / 3304 (0.48%) | 8 / 3305 (0.24%) | |
| occurrences causally related to treatment / all | 0 / 18 | 0 / 8 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tension headache | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Transient ischaemic attack | | | |
| subjects affected / exposed | 12 / 3304 (0.36%) | 14 / 3305 (0.42%) | |
| occurrences causally related to treatment / all | 0 / 12 | 0 / 16 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Trigeminal neuralgia | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Visual field defect | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebrovascular accident | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Hepatic encephalopathy | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| **Blood and lymphatic system disorders** | | | |
| Iron deficiency anaemia | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 4 / 3305 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Aplastic anaemia | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Aplasia pure red cell | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anaemia of chronic disease | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anaemia | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 10 / 3305 (0.30%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 10 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lymphadenopathy | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nephrogenic anaemia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 3304 (0.06%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Normochromic normocytic anaemia | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Polycythaemia | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancytopenia | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ear and labyrinth disorders | | | |
| Vertigo positional | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Deafness unilateral | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sudden hearing loss | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vertigo | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 4 / 3304 (0.12%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Eye disorders | | | |
| Amaurosis fugax | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cataract | | | |
| subjects affected / exposed | 3 / 3304 (0.09%) | 3 / 3305 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diabetic eye disease | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diabetic retinopathy | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Glaucoma | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lacrimal disorder | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ulcerative keratitis | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Retinal tear | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3304 (0.00%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Retinal haemorrhage | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Retinal detachment | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Retinal artery occlusion | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Macular degeneration | | | |
| subjects affected / exposed | 3 / 3304 (0.09%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lens dislocation | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vision blurred | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vitreous haemorrhage | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Retinopathy proliferative | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Chronic gastrointestinal bleeding | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abdominal discomfort | | | |
| subjects affected / exposed | 3 / 3304 (0.09%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abdominal hernia | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abdominal incarcerated hernia | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abdominal mass | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abdominal pain | | | |
| subjects affected / exposed | 7 / 3304 (0.21%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 8 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anal fissure | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ascites | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Duodenal ulcer | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Duodenal obstruction | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diverticular perforation | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diarrhoea | | | |
| subjects affected / exposed | 3 / 3304 (0.09%) | 3 / 3305 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Crohn's disease | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Constipation | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colitis ischaemic | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colitis | | | |

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|---|---|---|---|
| subjects affected / exposed | 2 / 3304 (0.06%) | 3 / 3305 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Duodenal ulcer haemorrhage | | | |
| subjects affected / exposed | 3 / 3304 (0.09%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal obstruction | | | |
| subjects affected / exposed | 3 / 3304 (0.09%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal ischaemia | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 2 | |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 6 / 3304 (0.18%) | 3 / 3305 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Gastrointestinal fistula | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastritis | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 4 / 3305 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastric ulcer haemorrhage | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastric ulcer | | | |

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|---|---|---|---|
| subjects affected / exposed | 2 / 3304 (0.06%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastric haemorrhage | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal perforation | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Obstructive pancreatitis | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haematemesis | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemorrhoidal haemorrhage | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ileus | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ileus paralytic | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 3 / 3305 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 2 | |
| Inguinal hernia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 3 / 3304 (0.09%) | 4 / 3305 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Inguinal hernia, obstructive | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intestinal obstruction | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 4 / 3305 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Nausea | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mesenteric artery stenosis | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Melaena | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mechanical ileus | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lower gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 5 / 3304 (0.15%) | 4 / 3305 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 8 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Large intestinal obstruction | | | |

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|---|---|---|---|
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Jejunal perforation | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intestinal polyp | | | |
| subjects affected / exposed | 4 / 3304 (0.12%) | 7 / 3305 (0.21%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 8 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Small intestinal obstruction | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Pancreatitis chronic | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancreatitis acute | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancreatitis | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 5 / 3305 (0.15%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancreatic mass | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancreatic cyst | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oesophagitis | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oesophageal varices haemorrhage | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Umbilical hernia | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 10 / 3305 (0.30%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 10 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | |
| Varices oesophageal | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vomiting | | | |
| subjects affected / exposed | 4 / 3304 (0.12%) | 3 / 3305 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Retroperitoneal fibrosis | | | |

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|---|---|---|---|
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Angioedema | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diabetic foot | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diabetic neuropathic ulcer | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diabetic ulcer | | | |
| subjects affected / exposed | 3 / 3304 (0.09%) | 6 / 3305 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Drug reaction with eosinophilia and systemic symptoms | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Eczema | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Henoch-Schonlein purpura | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pemphigoid | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rash | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rash vesicular | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin haemorrhage | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin irritation | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin ulcer | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Stevens-Johnson syndrome | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 93 / 3304 (2.81%) | 117 / 3305 (3.54%) | |
| occurrences causally related to treatment / all | 7 / 98 | 2 / 128 | |
| deaths causally related to treatment / all | 0 / 12 | 0 / 14 | |
| Calculus urethral | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Calculus urinary | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diabetic end stage renal disease | | | |
| subjects affected / exposed | 5 / 3304 (0.15%) | 4 / 3305 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diabetic nephropathy | | | |
| subjects affected / exposed | 4 / 3304 (0.12%) | 9 / 3305 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 12 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| End stage renal disease | | | |
| subjects affected / exposed | 35 / 3304 (1.06%) | 27 / 3305 (0.82%) | |
| occurrences causally related to treatment / all | 0 / 37 | 1 / 30 | |
| deaths causally related to treatment / all | 0 / 4 | 0 / 3 | |
| Focal segmental glomerulosclerosis | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Glomerulonephritis | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Glomerulonephritis membranoproliferative | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Glomerulonephritis membranous | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 3 / 3304 (0.09%) | 7 / 3305 (0.21%) | |
| occurrences causally related to treatment / all | 1 / 7 | 0 / 8 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haematuria | | | |
| subjects affected / exposed | 3 / 3304 (0.09%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hydronephrosis | | | |
| subjects affected / exposed | 4 / 3304 (0.12%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| IgA nephropathy | | | |
| subjects affected / exposed | 4 / 3304 (0.12%) | 5 / 3305 (0.15%) | |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lupus nephritis | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nephrolithiasis | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nephrotic syndrome | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oliguria | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Paraneoplastic nephrotic syndrome | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal artery stenosis | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal colic | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal cyst | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal disorder | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal impairment | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Stress urinary incontinence | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tubulointerstitial nephritis | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ureteric obstruction | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ureteric stenosis | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urethral stenosis | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary bladder polyp | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary retention | | | |
| subjects affected / exposed | 3 / 3304 (0.09%) | 3 / 3305 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| **Endocrine disorders** | | | |
| Hyperthyroidism | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypothyroidism | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thyroiditis | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| **Musculoskeletal and connective tissue disorders** | | | |

| | | | |
|---|---|---|---|
| Arthritis | | | |
| subjects affected / exposed | 3 / 3304 (0.09%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Back pain | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 5 / 3305 (0.15%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bone pain | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bursitis | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fibromyalgia | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gouty arthritis | | | |
| subjects affected / exposed | 3 / 3304 (0.09%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intervertebral disc disorder | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 3 / 3305 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Joint destruction | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Joint effusion | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 3304 (0.03%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mobility decreased | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Muscle atrophy | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Muscular weakness | | | |
| subjects affected / exposed | 3 / 3304 (0.09%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteoarthritis | | | |
| subjects affected / exposed | 4 / 3304 (0.12%) | 10 / 3305 (0.30%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 10 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteonecrosis | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Polymyalgia rheumatica | | | |
| subjects affected / exposed | 4 / 3304 (0.12%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rhabdomyolysis | | | |

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|---|---|---|---|
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rheumatoid arthritis | | | |
| subjects affected / exposed | 3 / 3304 (0.09%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal column stenosis | | | |
| subjects affected / exposed | 3 / 3304 (0.09%) | 4 / 3305 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spondyloarthropathy | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Synovitis | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tendonitis | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| **Infections and infestations** | | | |
| Arthritis infective | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Appendicitis | | | |
| subjects affected / exposed | 5 / 3304 (0.15%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abscess soft tissue | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 3304 (0.06%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abscess | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abdominal sepsis | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 2 | 0 / 1 | |
| Abdominal abscess | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Bacterial infection | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bacterial sepsis | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bone abscess | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchitis | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 4 / 3305 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchitis bacterial | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Campylobacter gastroenteritis | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Candida infection | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac valve abscess | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cellulitis | | | |
| subjects affected / exposed | 9 / 3304 (0.27%) | 12 / 3305 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 12 | 0 / 13 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Cellulitis gangrenous | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Clostridium colitis | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Clostridium difficile colitis | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Corona virus infection | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 98 / 3304 (2.97%) | 107 / 3305 (3.24%) | |
| occurrences causally related to treatment / all | 0 / 99 | 0 / 111 | |
| deaths causally related to treatment / all | 0 / 17 | 0 / 20 | |
| Cystitis | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Device related infection | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diabetic foot infection | | | |
| subjects affected / exposed | 17 / 3304 (0.51%) | 6 / 3305 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 18 | 0 / 7 | |
| deaths causally related to treatment / all | 0 / 2 | 0 / 0 | |
| Diabetic gangrene | | | |
| subjects affected / exposed | 4 / 3304 (0.12%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Epstein-Barr virus infection | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haematoma infection | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Endocarditis bacterial | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 3 / 3305 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Endocarditis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3304 (0.00%) | 3 / 3305 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 2 | |
| Empyema | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ear infection | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diverticulitis | | | |
| subjects affected / exposed | 7 / 3304 (0.21%) | 6 / 3305 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 7 | 0 / 7 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diarrhoea infectious | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Escherichia sepsis | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gallbladder empyema | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gangrene | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 8 / 3304 (0.24%) | 10 / 3305 (0.30%) | |
| occurrences causally related to treatment / all | 0 / 8 | 0 / 11 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis salmonella | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal bacterial infection | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal infection | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Genital infection fungal | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Enterobacter sepsis | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Labyrinthitis | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Joint abscess | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Inguinal hernia gangrenous | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Influenza | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infective exacerbation of chronic obstructive airways disease | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infected skin ulcer | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Herpes zoster | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 3 / 3305 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Helicobacter gastritis | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Laryngitis bacterial | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neutropenic sepsis | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Necrotising soft tissue infection | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Nail infection | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Muscle abscess | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Meningoencephalitis bacterial | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Lymphangitis | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lower respiratory tract infection bacterial | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 4 / 3304 (0.12%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Localised infection | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oral infection | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia bacterial | | | |
| subjects affected / exposed | 7 / 3304 (0.21%) | 4 / 3305 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 7 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 2 | 0 / 0 | |
| Osteomyelitis | | | |
| subjects affected / exposed | 3 / 3304 (0.09%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteomyelitis acute | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteomyelitis bacterial | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteomyelitis chronic | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia | | | |
| subjects affected / exposed | 39 / 3304 (1.18%) | 42 / 3305 (1.27%) | |
| occurrences causally related to treatment / all | 0 / 39 | 0 / 47 | |
| deaths causally related to treatment / all | 0 / 6 | 0 / 9 | |
| Pleural infection | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peritonitis bacterial | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 3304 (0.00%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peritonitis | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Perirectal abscess | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Periodontitis | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Perineal abscess | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancreatic abscess | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Otitis externa | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Orchitis | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rectal abscess | | | |

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|---|---|---|---|
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal abscess | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory tract infection | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 4 / 3305 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory tract infection viral | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia klebsiella | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia staphylococcal | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Pneumonia streptococcal | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia viral | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Postoperative wound infection | | | |

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|---|---|---|---|
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Prostate infection | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pseudomembranous colitis | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pseudomonas infection | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psoas abscess | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary tuberculosis | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyelocystitis | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyelonephritis | | | |
| subjects affected / exposed | 3 / 3304 (0.09%) | 3 / 3305 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 3 | 1 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | |
| Pyelonephritis acute | | | |

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|---|---|---|---|
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Severe invasive streptococcal infection | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 4 / 3304 (0.12%) | 3 / 3305 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sepsis | | | |
| subjects affected / exposed | 8 / 3304 (0.24%) | 6 / 3305 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 8 | 0 / 6 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | |
| Retroperitoneal abscess | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin bacterial infection | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin infection | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Soft tissue infection | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Spinal cord abscess | | | |

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|---|---|---|---|
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Staphylococcal infection | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Staphylococcal sepsis | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Staphylococcal skin infection | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Streptococcal infection | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Streptococcal sepsis | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Subcutaneous abscess | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Systemic bacterial infection | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thrombophlebitis septic | | | |

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|---|---|---|---|
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tonsillitis | | | |
| subjects affected / exposed | 3 / 3304 (0.09%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Septic shock | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Urosepsis | | | |
| subjects affected / exposed | 6 / 3304 (0.18%) | 5 / 3305 (0.15%) | |
| occurrences causally related to treatment / all | 1 / 7 | 2 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract infection bacterial | | | |
| subjects affected / exposed | 7 / 3304 (0.21%) | 6 / 3305 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 7 | 0 / 6 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 27 / 3304 (0.82%) | 31 / 3305 (0.94%) | |
| occurrences causally related to treatment / all | 2 / 29 | 0 / 33 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper respiratory tract infection bacterial | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Viral diarrhoea | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Wound sepsis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 3304 (0.06%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Wound infection bacterial | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Wound infection | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Wound abscess | | | |
| subjects affected / exposed | 2 / 3304 (0.06%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Viral infection | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 2 / 3305 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Viral pericarditis | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Viral pharyngitis | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| **Metabolism and nutrition disorders** | | | |
| Dehydration | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 22 / 3304 (0.67%) | 20 / 3305 (0.61%) | |
| occurrences causally related to treatment / all | 0 / 23 | 0 / 20 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diabetes mellitus | | | |
| subjects affected / exposed | 19 / 3304 (0.58%) | 23 / 3305 (0.70%) | |
| occurrences causally related to treatment / all | 0 / 19 | 0 / 23 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diabetes mellitus inadequate control | | | |
| subjects affected / exposed | 5 / 3304 (0.15%) | 6 / 3305 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diabetic ketoacidosis | | | |
| subjects affected / exposed | 5 / 3304 (0.15%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Electrolyte imbalance | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fluid overload | | | |
| subjects affected / exposed | 4 / 3304 (0.12%) | 9 / 3305 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 10 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fluid retention | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 3 / 3305 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gout | | | |
| subjects affected / exposed | 5 / 3304 (0.15%) | 5 / 3305 (0.15%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypercalcaemia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 8 / 3304 (0.24%) | 14 / 3305 (0.42%) | |
| occurrences causally related to treatment / all | 0 / 8 | 0 / 15 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyperglycaemic hyperosmolar nonketotic syndrome | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 4 / 3305 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyperkalaemia | | | |
| subjects affected / exposed | 14 / 3304 (0.42%) | 14 / 3305 (0.42%) | |
| occurrences causally related to treatment / all | 0 / 14 | 0 / 14 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Hypocalcaemia | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypoglycaemia | | | |
| subjects affected / exposed | 12 / 3304 (0.36%) | 11 / 3305 (0.33%) | |
| occurrences causally related to treatment / all | 0 / 12 | 1 / 12 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypokalaemia | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyponatraemia | | | |
| subjects affected / exposed | 3 / 3304 (0.09%) | 5 / 3305 (0.15%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypovolaemia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 4 / 3304 (0.12%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Insulin-requiring type 2 diabetes mellitus | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ketoacidosis | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ketosis | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 0 / 3305 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Malnutrition | | | |
| subjects affected / exposed | 1 / 3304 (0.03%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolic acidosis | | | |
| subjects affected / exposed | 6 / 3304 (0.18%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Type 2 diabetes mellitus | | | |
| subjects affected / exposed | 8 / 3304 (0.24%) | 9 / 3305 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 8 | 0 / 10 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Uraemic acidosis | | | |
| subjects affected / exposed | 0 / 3304 (0.00%) | 1 / 3305 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| **Non-serious adverse events** | Empa 10mg | Placebo | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 228 / 3304 (6.90%) | 262 / 3305 (7.93%) | |
| Metabolism and nutrition disorders | | | |
| Gout | | | |
| subjects affected / exposed | 228 / 3304 (6.90%) | 262 / 3305 (7.93%) | |
| occurrences (all) | 314 | 381 | |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 13 January 2020 | The recruitment target was increased to at least 6000 participants. Further exclusion of participation from people with type 1 diabetes was specified after introduction of a cap. Clarification was provided regarding the subdivisions of cardiovascular (CV) death. Tertiary subgroup analyses were restricted solely to the primary outcome and subgroups of key interest were specified. |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported