# Clinical trial results:
# A Phase 3, Randomized, Open Label Trial of Lenalidomide/dexamethasone With or Without Elotuzumab in Subjects with Previously Untreated Multiple Myeloma

## Summary

| | |
|---|---|
| EudraCT number | 2010-022445-20 |
| Trial protocol | CZ HU IE GB DE ES BE AT GR IT PL |
| Global end of trial date | 03 September 2021 |

### Results information

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 20 September 2022 |
| First version publication date | 20 September 2022 |

## Trial information

### Trial identification

| | |
|---|---|
| Sponsor protocol code | CA204-006 |

### Additional study identifiers

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

Notes:

### Sponsors

| | |
|---|---|
| Sponsor organisation name | Bristol-Myers Squibb |
| Sponsor organisation address | Chaussée de la Hulpe 185, Brussels, Belgium, 1170 |
| Public contact | EU Study Start-Up Unit, Bristol-Myers Squibb International Corporation, Clinical.Trials@bms.com |
| Scientific contact | Bristol-Myers Squibb Study Director, Bristol-Myers Squibb, Clinical.Trials@bms.com |

Notes:

### Paediatric regulatory details

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

Notes:

## Results analysis stage

| | |
|---|---|
| Analysis stage | Final |
| Date of interim/final analysis | 04 March 2022 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 03 September 2021 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

To compare PFS of lenalidomide/dexamethasone + elotuzumab (E-Ld) versus lenalidomide/dexamethasone (Ld) in subjects with newly diagnosed, untreated multiple myeloma (MM).

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization Good Clinical Practice Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 18 May 2011 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Australia: 42 |
| Country: Number of subjects enrolled | Austria: 7 |
| Country: Number of subjects enrolled | Belgium: 20 |
| Country: Number of subjects enrolled | Canada: 77 |
| Country: Number of subjects enrolled | Czechia: 12 |
| Country: Number of subjects enrolled | Germany: 35 |
| Country: Number of subjects enrolled | Greece: 68 |
| Country: Number of subjects enrolled | Hungary: 16 |
| Country: Number of subjects enrolled | Ireland: 6 |
| Country: Number of subjects enrolled | Israel: 28 |
| Country: Number of subjects enrolled | Italy: 95 |
| Country: Number of subjects enrolled | Poland: 72 |
| Country: Number of subjects enrolled | Romania: 20 |
| Country: Number of subjects enrolled | Russian Federation: 3 |
| Country: Number of subjects enrolled | Spain: 53 |
| Country: Number of subjects enrolled | Switzerland: 5 |
| Country: Number of subjects enrolled | Turkey: 5 |
| Country: Number of subjects enrolled | United Kingdom: 9 |
| Country: Number of subjects enrolled | United States: 175 |

| | |
|---|---|
| Worldwide total number of subjects | 748 |
| EEA total number of subjects | 404 |

Notes:

| **Subjects enrolled per age group** | |
|---|---|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 40 |
| From 65 to 84 years | 677 |
| 85 years and over | 31 |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

- E-Ld cohort: 374 participants were randomized.
371 participants entered the treatment period.
- Ld cohort: 374 participants were randomized.
371 participants entered the treatment period.

### Period 1

| | |
|---|---|
| Period 1 title | Pre-treatment period |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | E-Ld cohort |

Arm description:

Participants receiving a combination of Elotuzumab (E) Lenalidomide (L) Dexamethasone (d) in a 28 day cycle

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Elotuzumab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

20 mL Vial

| | |
|---|---|
| Investigational medicinal product name | Lenalidomide |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

5 mg, 10 mg, 15 mg and 25 mg Capsules

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

Dosage and administration details:

2 mg and 4 mg & various strengths

| | |
|---|---|
| Investigational medicinal product name | Dexamethosone |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravascular use |

Dosage and administration details:

4 mg/ml, 8 mg/ml & various strengths

| **Arm title** | Ld cohort |
|---|---|
| Arm description:<br>Participants receiving a combination of Lenalidomide (L) Dexamethasone (d) in a 28 day cycle | |
| Arm type | Active comparator |
| Investigational medicinal product name | Lenalidomide |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |
| Dosage and administration details:<br>5 mg, 10 mg, 15 mg and 25 mg Capsules | |
| Investigational medicinal product name | Dexamethosone |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravascular use |
| Dosage and administration details:<br>4 mg/ml, 8 mg/ml & various strengths | |
| Investigational medicinal product name | Dexamethasone |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |
| Dosage and administration details:<br>2 mg and 4 mg & various strengths | |

| **Number of subjects in period 1** | E-Ld cohort | Ld cohort |
|---|---|---|
| Started | 374 | 374 |
| Completed | 371 | 371 |
| Not completed | 3 | 3 |
| Consent withdrawal | 3 | - |
| No longer meeting study criteria | - | 1 |
| Participant request to discontinue | - | 1 |
| Adverse event unrelated to study drug | - | 1 |

| **Period 2** | |
|---|---|
| Period 2 title | Treatment period |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

## Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | E-Ld cohort |

Arm description:

Participants receiving a combination of Elotuzumab (E) Lenalidomide (L) Dexamethasone (d) in a 28 day cycle

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Elotuzumab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder for solution for infusion |
| Routes of administration | Intravascular use |

Dosage and administration details:

400 mg/vial

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

Dosage and administration details:

2 mg and 4 mg & various strengths

| | |
|---|---|
| Investigational medicinal product name | Dexamethosone |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravascular use |

Dosage and administration details:

4 mg/ml, 8 mg/ml & various strengths

| | |
|---|---|
| Investigational medicinal product name | Lenalidomide |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

5 mg, 10 mg, 15 mg and 25 mg

| | |
|---|---|
| **Arm title** | Ld cohort |

Arm description:

Participants receiving a combination of Lenalidomide (L) Dexamethasone (d) in a 28 day cycle

| | |
|---|---|
| Arm type | Active comparator |
| Investigational medicinal product name | Lenalidomide |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

5 mg, 10 mg, 15 mg and 25 mg

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

| | |
|---|---|
| Dosage and administration details:<br>2 mg and 4 mg & various strengths | |
| Investigational medicinal product name | Dexamethosone |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravascular use |
| Dosage and administration details:<br>4 mg/ml, 8 mg/ml & various strengths | |

| **Number of subjects in period 2** | E-Ld cohort | Ld cohort |
|---|---|---|
| Started | 371 | 371 |
| Completed | 0 | 0 |
| Not completed | 371 | 371 |
| Adverse event, serious fatal | 7 | 6 |
| No longer meet study criteria | 1 | 1 |
| Disease progression | 117 | 145 |
| Consent withdrawal | 10 | 7 |
| Study drug toxicity | 52 | 64 |
| Participant request to discontinue | 30 | 22 |
| Maximum clinical benefit | 1 | 1 |
| Adverse event unrelated to study drug | 110 | 73 |
| Other reasons | 30 | 30 |
| Poor/Non-compliance | 3 | 4 |
| Administrative reasons by Sponsor | 8 | 16 |
| Lost to follow-up | 2 | 2 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | E-Ld cohort |
| Reporting group description: | |
| Participants receiving a combination of Elotuzumab (E) Lenalidomide (L) Dexamethasone (d) in a 28 day cycle | |
| Reporting group title | Ld cohort |
| Reporting group description: | |
| Participants receiving a combination of Lenalidomide (L) Dexamethasone (d) in a 28 day cycle | |

| Reporting group values | E-Ld cohort | Ld cohort | Total |
|---|---|---|---|
| Number of subjects | 374 | 374 | 748 |
| Age categorical<br>Units: Subjects | | | |
| Adults (18-64 years) | 20 | 20 | 40 |
| From 65-84 years | 341 | 336 | 677 |
| 85 years and over | 13 | 18 | 31 |
| Age Continuous<br>Units: Years | | | |
| arithmetic mean | 72.9 | 73.1 | |
| standard deviation | ± 6.58 | ± 6.70 | - |
| Sex: Female, Male<br>Units: Participants | | | |
| Female | 163 | 173 | 336 |
| Male | 211 | 201 | 412 |
| Race (NIH/OMB)<br>Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | 0 |
| Asian | 1 | 4 | 5 |
| Native Hawaiian or Other Pacific Islander | 0 | 1 | 1 |
| Black or African American | 13 | 16 | 29 |
| White | 360 | 351 | 711 |
| More than one race | 0 | 0 | 0 |
| Unknown or Not Reported | 0 | 2 | 2 |
| Ethnicity (NIH/OMB)<br>Units: Subjects | | | |
| Hispanic or Latino | 9 | 8 | 17 |
| Not Hispanic or Latino | 70 | 87 | 157 |
| Unknown or Not Reported | 295 | 279 | 574 |

## End points

| End points reporting groups | |
|---|---|
| Reporting group title | E-Ld cohort |
| Reporting group description: | |
| Participants receiving a combination of Elotuzumab (E) Lenalidomide (L) Dexamethasone (d) in a 28 day cycle | |
| Reporting group title | Ld cohort |
| Reporting group description: | |
| Participants receiving a combination of Lenalidomide (L) Dexamethasone (d) in a 28 day cycle | |
| Reporting group title | E-Ld cohort |
| Reporting group description: | |
| Participants receiving a combination of Elotuzumab (E) Lenalidomide (L) Dexamethasone (d) in a 28 day cycle | |
| Reporting group title | Ld cohort |
| Reporting group description: | |
| Participants receiving a combination of Lenalidomide (L) Dexamethasone (d) in a 28 day cycle | |

| Primary: Progression-Free Survival (PFS) | |
|---|---|
| End point title | Progression-Free Survival (PFS) |
| End point description: | |
| PFS is defined as the time from randomization to the date of the first documented tumor progression (as determined by the Independent Review Committee (IRC)) or death due to any cause.<br>The IRC conducted a blinded, independent review of the tumor assessments based on the European Group for Blood and Bone Marrow Transplant (EBMT) criteria.<br>Censoring rules applied:<br>- Participants receiving subsequent systemic anti-myeloma therapy prior to documented progression were censored at the date of the last adequate tumor assessment prior to new therapy.<br>- Participants who had an event (progression or death) > 10 weeks after their last tumor assessment were censored at their last adequate tumor assessment prior to the event.<br>- Participants without progression or death (and not receiving subsequent therapy prior to progression) were censored at their last adequate tumor assessment.<br>- Participants without any post-baseline tumor assessments were censored on the date of randomization | |
| End point type | Primary |
| End point timeframe: | |
| From randomization to date of first documented tumor progression or death due to any cause (up to 8 years) | |

| End point values | E-Ld cohort | Ld cohort | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 374 | 374 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 31.38 (26.18 to 36.80) | 29.47 (23.49 to 34.30) | | |

## Statistical analyses

| **Statistical analysis title** | Statistical Analaysis for PFS |
|---|---|
| Comparison groups | E-Ld cohort v Ld cohort |
| Number of subjects included in analysis | 748 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.4358 |
| Method | Stratified Log Rank |

| **Statistical analysis title** | Statistical Anlaysis of PFS |
|---|---|
| Comparison groups | E-Ld cohort v Ld cohort |
| Number of subjects included in analysis | 748 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.93 |
| Confidence interval | |
| level | 95.71 % |
| sides | 2-sided |
| lower limit | 0.77 |
| upper limit | 1.12 |

| **Secondary: Objective Response Rate (ORR)** | |
|---|---|
| End point title | Objective Response Rate (ORR) |
| End point description: | |
| ORR is defined as the percentage of participants with objective response among all randomized subjects. Participants with an objective response are those participants experiencing a partial response (PR) or better, based on Indipendent Review Committee (IRC) assessment, as per EBMT criteria. | |
| End point type | Secondary |
| End point timeframe: | |
| From randomization to primary completion date (approximately 8 years) | |

| **End point values** | E-Ld cohort | Ld cohort | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 374 | 374 | | |
| Units: Percent of Participants | | | | |
| number (confidence interval 95%) | 82.9 (78.7 to 86.6) | 79.4 (75.0 to 83.4) | | |

**Statistical analyses**

| **Statistical analysis title** | Statistical Analysis for ORR |
|---|---|
| Comparison groups | E-Ld cohort v Ld cohort |
| Number of subjects included in analysis | 748 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.2232 |
| Method | CMH ESTIMATE OF COMMON ODDS RATIO |
| Parameter estimate | CMH ESTIMATE OF COMMON ODDS RATIO |
| Point estimate | 1.26 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.87 |
| upper limit | 1.82 |

| **Secondary: Overall Survival (OS)** | |
|---|---|
| End point title | Overall Survival (OS) |
| End point description: | |
| Survival is defined as the time from randomization to the date of death. A participant who did not die had his or her survival duration censored at the date of last contact (‘last known date alive”). | |
| End point type | Secondary |
| End point timeframe: | |
| From randomization to the date of death (up to 8 years) | |

| **End point values** | E-Ld cohort | Ld cohort | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 374 | 374 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 60.42 (52.76 to 67.35) | 57.56 (48.95 to 66.56) | | |

**Statistical analyses**

| **Statistical analysis title** | Statistical Analysis for OS |
|---|---|
| Comparison groups | E-Ld cohort v Ld cohort |
| Number of subjects included in analysis | 748 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.8932 |
| Method | Stratified log rank test |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.99 |

| Confidence interval | |
|---|---|
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.82 |
| upper limit | 1.19 |

## Secondary: Mean Change from Baseline of Pain Severity Score and Pain Interference Score

| End point title | Mean Change from Baseline of Pain Severity Score and Pain Interference Score |
|---|---|

End point description:

Pain severity (sensory dimension) and pain interference (reactive dimension, assessing the degree to which pain interferes with function) are measured using the Brief Pain Inventory- Short Form (BPI-SF). BPI-SF numeric rating scale goes from 0 (No pain) to 10 (Pain as bad as you can imagine).

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

End point timeframe:

From Baseline to End of Treatment (approximately 8 years)

| End point values | E-Ld cohort | Ld cohort | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 374 | 374 | | |
| Units: Rating score | | | | |
| arithmetic mean (standard deviation) | | | | |
| Pain Severity | 0.02 (± 2.645) | -0.25 (± 2.721) | | |
| Pain Interference | 0.33 (± 3.077) | -0.18 (± 3.082) | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Progression Free Survival (PFS) Rate at Specific Time-points

| End point title | Progression Free Survival (PFS) Rate at Specific Time-points |
|---|---|

End point description:

PFS rate is defined as the proportion of participants experiencing PFS at the defined time-points.

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

End point timeframe:

From randomization to the specified time-point (up to 5 years)

| End point values | E-Ld cohort | Ld cohort | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 374 | 374 | | |
| Units: Percent of participants | | | | |
| number (confidence interval 95%) | | | | |
| 1 year | 0.77 (0.72 to 0.81) | 0.76 (0.71 to 0.80) | | |
| 2 year | 0.59 (0.53 to 0.64) | 0.55 (0.49 to 0.60) | | |
| 3 year | 0.46 (0.40 to 0.51) | 0.41 (0.35 to 0.46) | | |
| 4 year | 0.36 (0.31 to 0.41) | 0.33 (0.28 to 0.38) | | |
| 5 year | 0.26 (0.21 to 0.32) | 0.25 (0.20 to 0.30) | | |

## Statistical analyses

| Statistical analysis title | Statistical Analysis for PFS |
|---|---|
| Statistical analysis description:<br>Statistical Analysis for PFS at specific time points | |
| Comparison groups | E-Ld cohort v Ld cohort |
| Number of subjects included in analysis | 748 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.4358 |
| Method | Hazard Ratio |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.93 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.78 |
| upper limit | 1.12 |

## Adverse events

| Adverse events information | |
|---|---|
| Timeframe for reporting adverse events:<br>From first dose to 60 days after last dose (up to 93.3 months) | |
| Assessment type | Systematic |

| Dictionary used | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | MedDRA24.1 |

| Reporting groups | |
|---|---|
| Reporting group title | Ld Cohort |
| Reporting group description:<br>Participants receiving a combination of<br>Lenalidomide (L)<br>Dexamethasone (d)<br>in a 28 day cycle | |
| Reporting group title | E-Ld Cohort |
| Reporting group description:<br>Participants receiving a combination of<br>Elotuzumab (E)<br>Lenalidomide (L)<br>Dexamethasone (d)<br>in a 28 day cycle | |

| Serious adverse events | Ld Cohort | E-Ld Cohort | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 279 / 371 (75.20%) | 293 / 371 (78.98%) | |
| number of deaths (all causes) | 232 | 240 | |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Acute lymphocytic leukaemia | | | |
| subjects affected / exposed | 2 / 371 (0.54%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Adenocarcinoma metastatic | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Adenocarcinoma pancreas | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| 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 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Atypical fibroxanthoma | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Basal cell carcinoma | | | |
| subjects affected / exposed | 10 / 371 (2.70%) | 10 / 371 (2.70%) | |
| occurrences causally related to treatment / all | 6 / 11 | 6 / 14 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Basosquamous carcinoma | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bladder neoplasm | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bowen's disease | | | |
| subjects affected / exposed | 2 / 371 (0.54%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholangiocarcinoma | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Colon cancer | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colon cancer metastatic | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | |
| Hepatic cancer | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastric cancer | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | |
| Hepatocellular carcinoma | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intraductal proliferative breast lesion | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Keratoacanthoma | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Laryngeal cancer | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lip squamous cell carcinoma | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Laryngeal squamous cell carcinoma | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lung adenocarcinoma | | | |
| subjects affected / exposed | 2 / 371 (0.54%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Malignant melanoma | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Malignant melanoma in situ | | | |
| subjects affected / exposed | 2 / 371 (0.54%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Malignant neoplasm progression | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Myelodysplastic syndrome | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nasal cavity cancer | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancreatic carcinoma | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Papilloma | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Plasma cell leukaemia | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Plasma cell myeloma | | | |
| subjects affected / exposed | 3 / 371 (0.81%) | 5 / 371 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 2 | 0 / 3 | |
| Plasmacytoma | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Prostate cancer | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 5 / 371 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rectal cancer | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rectosigmoid cancer | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Refractory anaemia with ringed sideroblasts | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sebaceous carcinoma | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spindle cell sarcoma | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| 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 | 7 / 371 (1.89%) | 13 / 371 (3.50%) | |
| occurrences causally related to treatment / all | 5 / 9 | 6 / 21 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Squamous cell carcinoma of skin | | | |
| subjects affected / exposed | 7 / 371 (1.89%) | 9 / 371 (2.43%) | |
| occurrences causally related to treatment / all | 3 / 14 | 4 / 12 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Squamous cell carcinoma of head and neck | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Transitional cell carcinoma | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | |
| Squamous cell carcinoma of the oral cavity | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |

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|---|---|---|---|
| Aortic aneurysm | | | |
| subjects affected / exposed | 2 / 371 (0.54%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Arteriosclerosis | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Circulatory collapse | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 10 / 371 (2.70%) | 9 / 371 (2.43%) | |
| occurrences causally related to treatment / all | 8 / 10 | 7 / 9 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Embolism | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 3 / 371 (0.81%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 2 | |
| Embolism venous | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haematoma | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypertension | | | |
| subjects affected / exposed | 2 / 371 (0.54%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypotension | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 371 (0.54%) | 7 / 371 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 2 | 1 / 7 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Hypovolaemic shock | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Malignant hypertension | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Orthostatic hypotension | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peripheral artery thrombosis | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peripheral ischaemia | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Superficial vein thrombosis | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thrombophlebitis | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 2 / 371 (0.54%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thrombosis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Venous thrombosis | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Adverse drug reaction | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Asthenia | | | |
| subjects affected / exposed | 6 / 371 (1.62%) | 3 / 371 (0.81%) | |
| occurrences causally related to treatment / all | 1 / 6 | 1 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chest pain | | | |
| subjects affected / exposed | 4 / 371 (1.08%) | 2 / 371 (0.54%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Complication associated with device | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Death | | | |
| subjects affected / exposed | 3 / 371 (0.81%) | 2 / 371 (0.54%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 3 | 0 / 2 | |
| Disease progression | | | |
| subjects affected / exposed | 5 / 371 (1.35%) | 8 / 371 (2.16%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 8 | |
| deaths causally related to treatment / all | 0 / 5 | 0 / 8 | |
| Fat necrosis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General physical health deterioration | | | |
| subjects affected / exposed | 5 / 371 (1.35%) | 3 / 371 (0.81%) | |
| occurrences causally related to treatment / all | 1 / 5 | 1 / 3 | |
| deaths causally related to treatment / all | 0 / 2 | 0 / 1 | |
| Fatigue | | | |
| subjects affected / exposed | 2 / 371 (0.54%) | 2 / 371 (0.54%) | |
| occurrences causally related to treatment / all | 0 / 2 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Inflammation | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 2 / 371 (0.54%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Malaise | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Multiple organ dysfunction syndrome | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 3 / 371 (0.81%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oedema peripheral | | | |
| subjects affected / exposed | 4 / 371 (1.08%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 2 / 4 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oedema | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 371 (0.27%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pain | | | |
| subjects affected / exposed | 3 / 371 (0.81%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Performance status decreased | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyrexia | | | |
| subjects affected / exposed | 7 / 371 (1.89%) | 19 / 371 (5.12%) | |
| occurrences causally related to treatment / all | 1 / 7 | 11 / 21 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sudden cardiac death | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | |
| Sudden death | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 2 / 371 (0.54%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 2 | |
| Systemic inflammatory response syndrome | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Immune system disorders | | | |
| Drug hypersensitivity | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypersensitivity | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 371 (0.00%) | 2 / 371 (0.54%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Reproductive system and breast disorders | | | |
| Endometrial hyperplasia | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Uterine prolapse | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| 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 | 0 / 371 (0.00%) | 2 / 371 (0.54%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Acute respiratory failure | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 3 / 371 (0.81%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Bronchiectasis | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 14 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchopneumopathy | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Bronchospasm | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 7 / 371 (1.89%) | 3 / 371 (0.81%) | |
| occurrences causally related to treatment / all | 3 / 10 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cough | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dyspnoea | | | |
| subjects affected / exposed | 8 / 371 (2.16%) | 13 / 371 (3.50%) | |
| occurrences causally related to treatment / all | 1 / 8 | 3 / 15 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Epistaxis | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypoxia | | | |
| subjects affected / exposed | 2 / 371 (0.54%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Interstitial lung disease | | | |
| subjects affected / exposed | 3 / 371 (0.81%) | 3 / 371 (0.81%) | |
| occurrences causally related to treatment / all | 0 / 3 | 2 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pleural effusion | | | |
| subjects affected / exposed | 3 / 371 (0.81%) | 5 / 371 (1.35%) | |
| occurrences causally related to treatment / all | 1 / 3 | 0 / 7 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Pleuritic pain | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 4 / 371 (1.08%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 1 / 4 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumothorax | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary congestion | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 15 / 371 (4.04%) | 12 / 371 (3.23%) | |
| occurrences causally related to treatment / all | 14 / 15 | 9 / 13 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary oedema | | | |
| subjects affected / exposed | 4 / 371 (1.08%) | 3 / 371 (0.81%) | |
| occurrences causally related to treatment / all | 1 / 4 | 2 / 3 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | |
| Respiratory depression | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Respiratory disorder | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory distress | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 2 / 371 (0.54%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Respiratory failure | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 3 / 371 (0.81%) | 4 / 371 (1.08%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | |
| Restrictive pulmonary disease | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sinus disorder | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vocal cord disorder | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 2 / 371 (0.54%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Completed suicide | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Confusional state | | | |
| subjects affected / exposed | 5 / 371 (1.35%) | 5 / 371 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Delirium | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 2 / 371 (0.54%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Delusional disorder, unspecified type | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Depression | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 2 / 371 (0.54%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mental status changes | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychotic disorder | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Product issues | | | |
| Device dislocation | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 2 / 371 (0.54%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 4 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 3 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bacterial test positive | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Blood creatinine increased | | | |
| subjects affected / exposed | 2 / 371 (0.54%) | 2 / 371 (0.54%) | |
| occurrences causally related to treatment / all | 1 / 2 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| C-reactive protein increased | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemoglobin decreased | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatic enzyme increased | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Influenza A virus test positive | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Influenza B virus test positive | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Liver function test abnormal | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory syncytial virus test positive | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respirovirus test positive | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Transaminases increased | | | |
| subjects affected / exposed | 2 / 371 (0.54%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Viral test positive | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Weight decreased | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Accidental overdose | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Combined tibia-fibula fracture | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Comminuted fracture | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Extradural haematoma | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (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 | 3 / 371 (0.81%) | 3 / 371 (0.81%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Femoral neck fracture | | | |
| subjects affected / exposed | 2 / 371 (0.54%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Femur fracture | | | |
| subjects affected / exposed | 8 / 371 (2.16%) | 4 / 371 (1.08%) | |
| occurrences causally related to treatment / all | 0 / 9 | 0 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fibula fracture | | | |
| subjects affected / exposed | 2 / 371 (0.54%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fracture | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 3 / 371 (0.81%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Head injury | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hip fracture | | | |
| subjects affected / exposed | 4 / 371 (1.08%) | 5 / 371 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Humerus fracture | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Joint injury | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infusion related reaction | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lumbar vertebral fracture | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Medication error | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| 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 | 2 / 371 (0.54%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Overdose | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 2 / 371 (0.54%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Post procedural complication | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Rib fracture | | | |
| subjects affected / exposed | 4 / 371 (1.08%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Shunt malfunction | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin laceration | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal compression fracture | | | |
| subjects affected / exposed | 4 / 371 (1.08%) | 2 / 371 (0.54%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal fracture | | | |
| subjects affected / exposed | 3 / 371 (0.81%) | 2 / 371 (0.54%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Stress fracture | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Subdural haematoma | | | |
| subjects affected / exposed | 2 / 371 (0.54%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | |
| Thoracic vertebral fracture | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tibia fracture | | | |
| subjects affected / exposed | 2 / 371 (0.54%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Traumatic fracture | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 371 (0.54%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Wrist fracture | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper limb fracture | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Congenital, familial and genetic disorders | | | |
| Corneal dystrophy | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Acute coronary syndrome | | | |
| subjects affected / exposed | 2 / 371 (0.54%) | 2 / 371 (0.54%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 7 / 371 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 7 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Angina pectoris | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 2 / 371 (0.54%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Angina unstable | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Aortic valve calcification | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Aortic valve incompetence | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Arrhythmia | | | |
| subjects affected / exposed | 2 / 371 (0.54%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 2 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 1 / 1 | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 12 / 371 (3.23%) | 22 / 371 (5.93%) | |
| occurrences causally related to treatment / all | 4 / 14 | 3 / 26 | |
| deaths causally related to treatment / all | 0 / 0 | 1 / 2 | |
| Atrial flutter | | | |
| subjects affected / exposed | 3 / 371 (0.81%) | 4 / 371 (1.08%) | |
| occurrences causally related to treatment / all | 1 / 3 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrial tachycardia | | | |
| subjects affected / exposed | 2 / 371 (0.54%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrial thrombosis | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrioventricular block | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bradycardia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac arrest | | | |
| subjects affected / exposed | 6 / 371 (1.62%) | 7 / 371 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 7 | |
| deaths causally related to treatment / all | 0 / 6 | 0 / 6 | |
| Cardiac failure | | | |
| subjects affected / exposed | 7 / 371 (1.89%) | 13 / 371 (3.50%) | |
| occurrences causally related to treatment / all | 0 / 7 | 1 / 16 | |
| deaths causally related to treatment / all | 0 / 2 | 0 / 4 | |
| Cardiac failure acute | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Cardiac failure chronic | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac failure congestive | | | |
| subjects affected / exposed | 4 / 371 (1.08%) | 4 / 371 (1.08%) | |
| occurrences causally related to treatment / all | 2 / 4 | 2 / 6 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Cardiac septal hypertrophy | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac ventricular thrombosis | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiogenic shock | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Cardio-respiratory arrest | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | |
| Cardiomyopathy | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiopulmonary failure | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Cardiovascular disorder | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 2 / 371 (0.54%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 2 | |
| Congestive cardiomyopathy | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Coronary artery disease | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 2 / 371 (0.54%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Left ventricular dysfunction | | | |
| subjects affected / exposed | 2 / 371 (0.54%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mitral valve incompetence | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 371 (0.00%) | 2 / 371 (0.54%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Myocardial infarction | | | |
| subjects affected / exposed | 5 / 371 (1.35%) | 6 / 371 (1.62%) | |
| occurrences causally related to treatment / all | 1 / 5 | 0 / 6 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 2 | |
| Pericarditis | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myocardial ischaemia | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 2 / 371 (0.54%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Prinzmetal angina | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sinus arrest | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sinus node dysfunction | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 3 / 371 (0.81%) | |
| occurrences causally related to treatment / all | 0 / 1 | 2 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sinus tachycardia | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Systolic dysfunction | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Supraventricular tachycardia | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tachycardia | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 3 / 371 (0.81%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Torsade de pointes | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ventricular arrhythmia | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Ataxia | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Carotid artery stenosis | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebellar haemorrhage | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebral haemorrhage | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 3 / 371 (0.81%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 2 | 0 / 0 | |
| Cerebral infarction | | | |
| subjects affected / exposed | 2 / 371 (0.54%) | 2 / 371 (0.54%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebral ischaemia | | | |
| subjects affected / exposed | 2 / 371 (0.54%) | 3 / 371 (0.81%) | |
| occurrences causally related to treatment / all | 0 / 2 | 2 / 3 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 7 / 371 (1.89%) | 8 / 371 (2.16%) | |
| occurrences causally related to treatment / all | 5 / 8 | 3 / 8 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | |
| Coma | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cognitive disorder | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dementia | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Depressed level of consciousness | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dizziness | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 371 (0.27%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dizziness postural | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Encephalopathy | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dysarthria | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 2 / 371 (0.54%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Generalised tonic-clonic seizure | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Guillain-Barre syndrome | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemorrhage intracranial | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemorrhagic cerebral infarction | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (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 | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Headache | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intracranial aneurysm | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intracranial haematoma | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ischaemic cerebral infarction | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ischaemic stroke | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 4 / 371 (1.08%) | |
| occurrences causally related to treatment / all | 0 / 1 | 2 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Lethargy | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Loss of consciousness | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Memory impairment | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolic encephalopathy | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (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 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myelopathy | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Normal pressure hydrocephalus | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Presyncope | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 2 / 371 (0.54%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sciatica | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal cord compression | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Somnolence | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Subarachnoid haemorrhage | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 2 / 371 (0.54%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Syncope | | | |
| subjects affected / exposed | 5 / 371 (1.35%) | 7 / 371 (1.89%) | |
| occurrences causally related to treatment / all | 0 / 5 | 2 / 7 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Transient aphasia | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Transient ischaemic attack | | | |
| subjects affected / exposed | 4 / 371 (1.08%) | 6 / 371 (1.62%) | |
| occurrences causally related to treatment / all | 0 / 4 | 1 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| **Blood and lymphatic system disorders** | | | |
| Agranulocytosis | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anaemia | | | |
| subjects affected / exposed | 12 / 371 (3.23%) | 12 / 371 (3.23%) | |
| occurrences causally related to treatment / all | 4 / 17 | 5 / 16 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Febrile neutropenia | | | |
| subjects affected / exposed | 3 / 371 (0.81%) | 5 / 371 (1.35%) | |
| occurrences causally related to treatment / all | 1 / 3 | 3 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemolysis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemolytic anaemia | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neutropenia | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancytopenia | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 4 / 371 (1.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Plasmacytosis | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 2 / 371 (0.54%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 2 / 2 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ear and labyrinth disorders | | | |
| Sudden hearing loss | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vertigo | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Eye disorders | | | |

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|---|---|---|---|
| Blindness transient | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cataract | | | |
| subjects affected / exposed | 9 / 371 (2.43%) | 10 / 371 (2.70%) | |
| occurrences causally related to treatment / all | 8 / 13 | 6 / 13 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cataract cortical | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Epiretinal membrane | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Optic ischaemic neuropathy | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Retinal detachment | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 2 / 371 (0.54%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 1 / 2 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abdominal pain lower | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abdominal pain upper | | | |

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|---|---|---|---|
| subjects affected / exposed | 1 / 371 (0.27%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anal haemorrhage | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anorectal varices haemorrhage | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colitis | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colitis ulcerative | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Constipation | | | |
| subjects affected / exposed | 2 / 371 (0.54%) | 3 / 371 (0.81%) | |
| occurrences causally related to treatment / all | 1 / 2 | 1 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diaphragmatic hernia | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diarrhoea | | | |
| subjects affected / exposed | 10 / 371 (2.70%) | 9 / 371 (2.43%) | |
| occurrences causally related to treatment / all | 3 / 11 | 2 / 10 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diverticulum intestinal | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Duodenal ulcer | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Enteritis | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Enterovesical fistula | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Femoral hernia | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastritis | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 4 / 371 (1.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 2 / 371 (0.54%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hiatus hernia | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ileus | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 371 (0.54%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Incarcerated inguinal hernia | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Incarcerated umbilical hernia | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Inguinal hernia | | | |
| subjects affected / exposed | 2 / 371 (0.54%) | 3 / 371 (0.81%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Inguinal hernia strangulated | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intestinal infarction | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intestinal obstruction | | | |
| subjects affected / exposed | 2 / 371 (0.54%) | 4 / 371 (1.08%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intestinal perforation | | | |
| subjects affected / exposed | 2 / 371 (0.54%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Large intestine polyp | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lower gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Melaena | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nausea | | | |
| subjects affected / exposed | 3 / 371 (0.81%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Odynophagia | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oesophageal ulcer | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oesophagitis | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oroantral fistula | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancreatitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 3 / 371 (0.81%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancreatitis acute | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumatosis intestinalis | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 2 / 371 (0.54%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Small intestinal obstruction | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Umbilical hernia | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Varices oesophageal | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vomiting | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 3 / 371 (0.81%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Bile duct stone | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Biliary obstruction | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholecystitis | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 2 / 371 (0.54%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholecystitis acute | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 2 / 371 (0.54%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholecystitis chronic | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholelithiasis | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gallbladder rupture | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hydrocholecystis | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Jaundice | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Actinic keratosis | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Angioedema | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cold sweat | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cutaneous vasculitis | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dermatitis bullous | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dermatitis exfoliative generalised | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diabetic foot | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Erythema | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Exfoliative rash | | | |
| subjects affected / exposed | 2 / 371 (0.54%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Purpura | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rash | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rash maculo-papular | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin ulcer | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Stasis dermatitis | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Subcutaneous emphysema | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Stevens-Johnson syndrome | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 20 / 371 (5.39%) | 20 / 371 (5.39%) | |
| occurrences causally related to treatment / all | 4 / 21 | 4 / 20 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 2 | |
| Calculus urinary | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chronic kidney disease | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 2 / 371 (0.54%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| End stage renal disease | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myeloma cast nephropathy | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Haematuria | | | |
| subjects affected / exposed | 2 / 371 (0.54%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal failure | | | |
| subjects affected / exposed | 7 / 371 (1.89%) | 10 / 371 (2.70%) | |
| occurrences causally related to treatment / all | 2 / 7 | 5 / 10 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nephrolithiasis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 371 (0.54%) | 2 / 371 (0.54%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal impairment | | | |
| subjects affected / exposed | 3 / 371 (0.81%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 1 / 4 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal injury | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal tubular necrosis | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary retention | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 2 / 371 (0.54%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract disorder | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Endocrine disorders | | | |
| Adrenal insufficiency | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 2 / 371 (0.54%) | 2 / 371 (0.54%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Arthritis | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Arthritis reactive | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Back pain | | | |
| subjects affected / exposed | 9 / 371 (2.43%) | 11 / 371 (2.96%) | |
| occurrences causally related to treatment / all | 0 / 11 | 0 / 14 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bone pain | | | |
| subjects affected / exposed | 4 / 371 (1.08%) | 3 / 371 (0.81%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bursitis | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chondrocalcinosis | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chondrocalcinosis pyrophosphate | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intervertebral disc protrusion | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Flank pain | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Muscle contracture | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Joint hyperextension | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Muscular weakness | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal disorder | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteitis | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteoarthritis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 371 (0.00%) | 3 / 371 (0.81%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteonecrosis | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 2 / 371 (0.54%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteonecrosis of jaw | | | |
| subjects affected / exposed | 2 / 371 (0.54%) | 3 / 371 (0.81%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pain in extremity | | | |
| subjects affected / exposed | 2 / 371 (0.54%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pathological fracture | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal pain | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 3 / 371 (0.81%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal stenosis | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Abdominal abscess | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abscess limb | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abscess | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atypical pneumonia | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Bacteraemia | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bacterial prostatitis | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Biliary sepsis | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchitis | | | |
| subjects affected / exposed | 6 / 371 (1.62%) | 18 / 371 (4.85%) | |
| occurrences causally related to treatment / all | 1 / 6 | 6 / 20 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bursitis infective | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cellulitis | | | |
| subjects affected / exposed | 8 / 371 (2.16%) | 9 / 371 (2.43%) | |
| occurrences causally related to treatment / all | 1 / 9 | 0 / 9 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cellulitis orbital | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Central nervous system infection | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Clostridial sepsis | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Clostridium colitis | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Clostridium difficile colitis | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 2 / 371 (0.54%) | |
| occurrences causally related to treatment / all | 0 / 2 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Clostridium difficile infection | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 2 / 371 (0.54%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dacryocystitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Device related infection | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diverticulitis | | | |
| subjects affected / exposed | 3 / 371 (0.81%) | 5 / 371 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 3 | 4 / 10 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Erysipelas | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 2 / 371 (0.54%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Escherichia bacteraemia | | | |
| subjects affected / exposed | 2 / 371 (0.54%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Escherichia infection | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Escherichia urinary tract infection | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Febrile infection | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 2 / 371 (0.54%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 371 (0.54%) | 8 / 371 (2.16%) | |
| occurrences causally related to treatment / all | 0 / 2 | 2 / 8 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis clostridial | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis salmonella | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal infection | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis viral | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| H1N1 influenza | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatitis E | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Herpes zoster | | | |
| subjects affected / exposed | 2 / 371 (0.54%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Herpes zoster disseminated | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infected cyst | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infection | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 4 / 371 (1.08%) | |
| occurrences causally related to treatment / all | 0 / 1 | 2 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infectious pleural effusion | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Influenza | | | |
| subjects affected / exposed | 6 / 371 (1.62%) | 7 / 371 (1.89%) | |
| occurrences causally related to treatment / all | 1 / 7 | 0 / 7 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intervertebral discitis | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Large intestine infection | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Leishmaniasis | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Liver abscess | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Localised infection | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Meningitis listeria | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 8 / 371 (2.16%) | 9 / 371 (2.43%) | |
| occurrences causally related to treatment / all | 4 / 8 | 1 / 10 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Metapneumovirus bronchiolitis | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metapneumovirus infection | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neutropenic sepsis | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Orchitis | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Perirectal abscess | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 371 (0.27%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peritonitis | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Pharyngitis | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Plague | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pleural infection | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Pneumococcal sepsis | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumocystis jirovecii pneumonia | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 2 / 371 (0.54%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Pneumonia | | | |
| subjects affected / exposed | 48 / 371 (12.94%) | 60 / 371 (16.17%) | |
| occurrences causally related to treatment / all | 11 / 58 | 21 / 80 | |
| deaths causally related to treatment / all | 1 / 5 | 2 / 10 | |
| Pneumonia aspiration | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 371 (0.00%) | 5 / 371 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 2 | |
| Pneumonia bacterial | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia cytomegaloviral | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia fungal | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 2 / 371 (0.54%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia influenzal | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia legionella | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Pneumonia staphylococcal | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | |
| Pneumonia streptococcal | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| 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 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Progressive multifocal leukoencephalopathy | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | |
| Pseudomembranous colitis | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyelonephritis | | | |
| subjects affected / exposed | 2 / 371 (0.54%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyoderma | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory syncytial virus infection | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory tract infection | | | |
| subjects affected / exposed | 3 / 371 (0.81%) | 8 / 371 (2.16%) | |
| occurrences causally related to treatment / all | 2 / 5 | 2 / 9 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Sepsis | | | |
| subjects affected / exposed | 6 / 371 (1.62%) | 15 / 371 (4.04%) | |
| occurrences causally related to treatment / all | 3 / 6 | 1 / 15 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 5 | |
| Septic shock | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 6 / 371 (1.62%) | 4 / 371 (1.08%) | |
| occurrences causally related to treatment / all | 2 / 6 | 0 / 4 | |
| deaths causally related to treatment / all | 2 / 5 | 0 / 4 | |
| Staphylococcal infection | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 2 / 371 (0.54%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Staphylococcal sepsis | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Subcutaneous abscess | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 4 / 371 (1.08%) | 5 / 371 (1.35%) | |
| occurrences causally related to treatment / all | 1 / 4 | 1 / 5 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 11 / 371 (2.96%) | 15 / 371 (4.04%) | |
| occurrences causally related to treatment / all | 3 / 13 | 2 / 19 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract infection bacterial | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract infection enterococcal | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urosepsis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 5 / 371 (1.35%) | 5 / 371 (1.35%) | |
| occurrences causally related to treatment / all | 2 / 5 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Varicella zoster virus infection | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular device infection | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Viral infection | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Whipple's disease | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Wound infection staphylococcal | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| **Metabolism and nutrition disorders** | | | |
| Alcohol intolerance | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Decreased appetite | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dehydration | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 5 / 371 (1.35%) | 7 / 371 (1.89%) | |
| occurrences causally related to treatment / all | 2 / 5 | 1 / 7 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diabetic complication | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diabetic ketoacidosis | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diabetic metabolic decompensation | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Electrolyte imbalance | | | |
| subjects affected / exposed | 2 / 371 (0.54%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Failure to thrive | | | |
| subjects affected / exposed | 2 / 371 (0.54%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 1 / 2 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gout | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypercalcaemia | | | |
| subjects affected / exposed | 5 / 371 (1.35%) | 2 / 371 (0.54%) | |
| occurrences causally related to treatment / all | 0 / 7 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyperglycaemia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 371 (0.54%) | 3 / 371 (0.81%) | |
| occurrences causally related to treatment / all | 2 / 2 | 3 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypervolaemia | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypoalbuminaemia | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypocalcaemia | | | |
| subjects affected / exposed | 4 / 371 (1.08%) | 4 / 371 (1.08%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypoglycaemia | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 5 / 371 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypokalaemia | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 4 / 371 (1.08%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypomagnesaemia | | | |
| subjects affected / exposed | 0 / 371 (0.00%) | 4 / 371 (1.08%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyponatraemia | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 2 / 371 (0.54%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypophosphataemia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 371 (0.00%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Malnutrition | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 0 / 371 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tumour lysis syndrome | | | |
| subjects affected / exposed | 1 / 371 (0.27%) | 1 / 371 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| **Non-serious adverse events** | Ld Cohort | E-Ld Cohort | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 365 / 371 (98.38%) | 364 / 371 (98.11%) | |
| Vascular disorders | | | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 26 / 371 (7.01%) | 20 / 371 (5.39%) | |
| occurrences (all) | 30 | 20 | |
| Flushing | | | |
| subjects affected / exposed | 17 / 371 (4.58%) | 19 / 371 (5.12%) | |
| occurrences (all) | 18 | 22 | |
| Hypertension | | | |
| subjects affected / exposed | 44 / 371 (11.86%) | 54 / 371 (14.56%) | |
| occurrences (all) | 60 | 100 | |
| Hypotension | | | |
| subjects affected / exposed | 44 / 371 (11.86%) | 63 / 371 (16.98%) | |
| occurrences (all) | 51 | 86 | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 73 / 371 (19.68%) | 88 / 371 (23.72%) | |
| occurrences (all) | 108 | 137 | |
| Chest pain | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 32 / 371 (8.63%) | 24 / 371 (6.47%) | |
| occurrences (all) | 39 | 30 | |
| Chills | | | |
| subjects affected / exposed | 9 / 371 (2.43%) | 35 / 371 (9.43%) | |
| occurrences (all) | 12 | 44 | |
| Fatigue | | | |
| subjects affected / exposed | 188 / 371 (50.67%) | 183 / 371 (49.33%) | |
| occurrences (all) | 279 | 288 | |
| Influenza like illness | | | |
| subjects affected / exposed | 28 / 371 (7.55%) | 40 / 371 (10.78%) | |
| occurrences (all) | 54 | 61 | |
| Mucosal inflammation | | | |
| subjects affected / exposed | 8 / 371 (2.16%) | 21 / 371 (5.66%) | |
| occurrences (all) | 8 | 28 | |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 19 / 371 (5.12%) | 20 / 371 (5.39%) | |
| occurrences (all) | 22 | 23 | |
| Oedema | | | |
| subjects affected / exposed | 19 / 371 (5.12%) | 17 / 371 (4.58%) | |
| occurrences (all) | 21 | 17 | |
| Oedema peripheral | | | |
| subjects affected / exposed | 182 / 371 (49.06%) | 163 / 371 (43.94%) | |
| occurrences (all) | 314 | 259 | |
| Pain | | | |
| subjects affected / exposed | 19 / 371 (5.12%) | 24 / 371 (6.47%) | |
| occurrences (all) | 36 | 27 | |
| Peripheral swelling | | | |
| subjects affected / exposed | 24 / 371 (6.47%) | 24 / 371 (6.47%) | |
| occurrences (all) | 30 | 25 | |
| Pyrexia | | | |
| subjects affected / exposed | 77 / 371 (20.75%) | 111 / 371 (29.92%) | |
| occurrences (all) | 167 | 211 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 106 / 371 (28.57%) | 120 / 371 (32.35%) | |
| occurrences (all) | 168 | 191 | |
| Dysphonia | | | |
| subjects affected / exposed | 27 / 371 (7.28%) | 45 / 371 (12.13%) | |
| occurrences (all) | 30 | 49 | |
| Dyspnoea | | | |
| subjects affected / exposed | 93 / 371 (25.07%) | 87 / 371 (23.45%) | |
| occurrences (all) | 122 | 118 | |
| Dyspnoea exertional | | | |
| subjects affected / exposed | 18 / 371 (4.85%) | 24 / 371 (6.47%) | |
| occurrences (all) | 20 | 30 | |
| Epistaxis | | | |
| subjects affected / exposed | 18 / 371 (4.85%) | 27 / 371 (7.28%) | |
| occurrences (all) | 26 | 33 | |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 26 / 371 (7.01%) | 26 / 371 (7.01%) | |
| occurrences (all) | 35 | 30 | |
| Productive cough | | | |
| subjects affected / exposed | 20 / 371 (5.39%) | 33 / 371 (8.89%) | |
| occurrences (all) | 24 | 43 | |
| Psychiatric disorders | | | |
| Agitation | | | |
| subjects affected / exposed | 17 / 371 (4.58%) | 21 / 371 (5.66%) | |
| occurrences (all) | 21 | 23 | |
| Anxiety | | | |
| subjects affected / exposed | 28 / 371 (7.55%) | 44 / 371 (11.86%) | |
| occurrences (all) | 33 | 50 | |
| Confusional state | | | |
| subjects affected / exposed | 32 / 371 (8.63%) | 37 / 371 (9.97%) | |
| occurrences (all) | 35 | 43 | |
| Depression | | | |
| subjects affected / exposed | 31 / 371 (8.36%) | 42 / 371 (11.32%) | |
| occurrences (all) | 35 | 45 | |
| Insomnia | | | |
| subjects affected / exposed | 96 / 371 (25.88%) | 98 / 371 (26.42%) | |
| occurrences (all) | 112 | 129 | |

| | | | |
|---|---|---|---|
| Mood altered | | | |
| subjects affected / exposed | 17 / 371 (4.58%) | 25 / 371 (6.74%) | |
| occurrences (all) | 33 | 26 | |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 27 / 371 (7.28%) | 18 / 371 (4.85%) | |
| occurrences (all) | 38 | 24 | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 21 / 371 (5.66%) | 17 / 371 (4.58%) | |
| occurrences (all) | 27 | 25 | |
| Blood creatinine increased | | | |
| subjects affected / exposed | 72 / 371 (19.41%) | 56 / 371 (15.09%) | |
| occurrences (all) | 111 | 85 | |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 28 / 371 (7.55%) | 11 / 371 (2.96%) | |
| occurrences (all) | 55 | 27 | |
| Glomerular filtration rate decreased | | | |
| subjects affected / exposed | 17 / 371 (4.58%) | 20 / 371 (5.39%) | |
| occurrences (all) | 35 | 37 | |
| Platelet count decreased | | | |
| subjects affected / exposed | 20 / 371 (5.39%) | 12 / 371 (3.23%) | |
| occurrences (all) | 58 | 17 | |
| Weight decreased | | | |
| subjects affected / exposed | 66 / 371 (17.79%) | 79 / 371 (21.29%) | |
| occurrences (all) | 78 | 93 | |
| Injury, poisoning and procedural complications | | | |
| Contusion | | | |
| subjects affected / exposed | 53 / 371 (14.29%) | 47 / 371 (12.67%) | |
| occurrences (all) | 72 | 60 | |
| Fall | | | |
| subjects affected / exposed | 32 / 371 (8.63%) | 33 / 371 (8.89%) | |
| occurrences (all) | 49 | 46 | |
| Skin abrasion | | | |
| subjects affected / exposed | 13 / 371 (3.50%) | 24 / 371 (6.47%) | |
| occurrences (all) | 15 | 29 | |
| Skin laceration | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 23 / 371 (6.20%) | 19 / 371 (5.12%) | |
| occurrences (all) | 31 | 26 | |
| Cardiac disorders | | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 25 / 371 (6.74%) | 28 / 371 (7.55%) | |
| occurrences (all) | 29 | 35 | |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 68 / 371 (18.33%) | 84 / 371 (22.64%) | |
| occurrences (all) | 102 | 124 | |
| Dysgeusia | | | |
| subjects affected / exposed | 13 / 371 (3.50%) | 26 / 371 (7.01%) | |
| occurrences (all) | 15 | 29 | |
| Headache | | | |
| subjects affected / exposed | 50 / 371 (13.48%) | 61 / 371 (16.44%) | |
| occurrences (all) | 73 | 85 | |
| Hypoaesthesia | | | |
| subjects affected / exposed | 25 / 371 (6.74%) | 24 / 371 (6.47%) | |
| occurrences (all) | 28 | 28 | |
| Memory impairment | | | |
| subjects affected / exposed | 15 / 371 (4.04%) | 27 / 371 (7.28%) | |
| occurrences (all) | 16 | 28 | |
| Neuropathy peripheral | | | |
| subjects affected / exposed | 48 / 371 (12.94%) | 41 / 371 (11.05%) | |
| occurrences (all) | 54 | 48 | |
| Paraesthesia | | | |
| subjects affected / exposed | 45 / 371 (12.13%) | 40 / 371 (10.78%) | |
| occurrences (all) | 55 | 65 | |
| Peripheral sensory neuropathy | | | |
| subjects affected / exposed | 59 / 371 (15.90%) | 57 / 371 (15.36%) | |
| occurrences (all) | 71 | 70 | |
| Syncope | | | |
| subjects affected / exposed | 20 / 371 (5.39%) | 18 / 371 (4.85%) | |
| occurrences (all) | 23 | 22 | |
| Taste disorder | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 27 / 371 (7.28%) | 24 / 371 (6.47%) | |
| occurrences (all) | 27 | 24 | |
| Tremor | | | |
| subjects affected / exposed | 55 / 371 (14.82%) | 61 / 371 (16.44%) | |
| occurrences (all) | 69 | 72 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 160 / 371 (43.13%) | 153 / 371 (41.24%) | |
| occurrences (all) | 325 | 338 | |
| Leukopenia | | | |
| subjects affected / exposed | 37 / 371 (9.97%) | 23 / 371 (6.20%) | |
| occurrences (all) | 141 | 83 | |
| Neutropenia | | | |
| subjects affected / exposed | 117 / 371 (31.54%) | 93 / 371 (25.07%) | |
| occurrences (all) | 397 | 286 | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 69 / 371 (18.60%) | 66 / 371 (17.79%) | |
| occurrences (all) | 153 | 178 | |
| Eye disorders | | | |
| Cataract | | | |
| subjects affected / exposed | 56 / 371 (15.09%) | 61 / 371 (16.44%) | |
| occurrences (all) | 64 | 70 | |
| Vision blurred | | | |
| subjects affected / exposed | 28 / 371 (7.55%) | 28 / 371 (7.55%) | |
| occurrences (all) | 30 | 29 | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 51 / 371 (13.75%) | 50 / 371 (13.48%) | |
| occurrences (all) | 66 | 76 | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 29 / 371 (7.82%) | 33 / 371 (8.89%) | |
| occurrences (all) | 37 | 40 | |
| Constipation | | | |
| subjects affected / exposed | 144 / 371 (38.81%) | 142 / 371 (38.27%) | |
| occurrences (all) | 215 | 230 | |
| Diarrhoea | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 180 / 371 (48.52%) | 192 / 371 (51.75%) | |
| occurrences (all) | 399 | 476 | |
| Dry mouth | | | |
| subjects affected / exposed | 26 / 371 (7.01%) | 28 / 371 (7.55%) | |
| occurrences (all) | 31 | 30 | |
| Dyspepsia | | | |
| subjects affected / exposed | 32 / 371 (8.63%) | 43 / 371 (11.59%) | |
| occurrences (all) | 34 | 58 | |
| Haemorrhoids | | | |
| subjects affected / exposed | 19 / 371 (5.12%) | 10 / 371 (2.70%) | |
| occurrences (all) | 21 | 10 | |
| Nausea | | | |
| subjects affected / exposed | 108 / 371 (29.11%) | 117 / 371 (31.54%) | |
| occurrences (all) | 161 | 189 | |
| Toothache | | | |
| subjects affected / exposed | 15 / 371 (4.04%) | 24 / 371 (6.47%) | |
| occurrences (all) | 18 | 30 | |
| Vomiting | | | |
| subjects affected / exposed | 50 / 371 (13.48%) | 69 / 371 (18.60%) | |
| occurrences (all) | 72 | 119 | |
| Skin and subcutaneous tissue disorders | | | |
| Dry skin | | | |
| subjects affected / exposed | 22 / 371 (5.93%) | 27 / 371 (7.28%) | |
| occurrences (all) | 24 | 27 | |
| Erythema | | | |
| subjects affected / exposed | 21 / 371 (5.66%) | 19 / 371 (5.12%) | |
| occurrences (all) | 24 | 19 | |
| Night sweats | | | |
| subjects affected / exposed | 15 / 371 (4.04%) | 24 / 371 (6.47%) | |
| occurrences (all) | 21 | 29 | |
| Hyperhidrosis | | | |
| subjects affected / exposed | 26 / 371 (7.01%) | 36 / 371 (9.70%) | |
| occurrences (all) | 32 | 43 | |
| Pruritus | | | |
| subjects affected / exposed | 43 / 371 (11.59%) | 39 / 371 (10.51%) | |
| occurrences (all) | 50 | 48 | |

| | | | |
|---|---|---|---|
| Rash | | | |
| subjects affected / exposed | 86 / 371 (23.18%) | 90 / 371 (24.26%) | |
| occurrences (all) | 113 | 132 | |
| Skin lesion | | | |
| subjects affected / exposed | 17 / 371 (4.58%) | 19 / 371 (5.12%) | |
| occurrences (all) | 21 | 25 | |
| Renal and urinary disorders | | | |
| Dysuria | | | |
| subjects affected / exposed | 19 / 371 (5.12%) | 16 / 371 (4.31%) | |
| occurrences (all) | 23 | 19 | |
| Pollakiuria | | | |
| subjects affected / exposed | 19 / 371 (5.12%) | 14 / 371 (3.77%) | |
| occurrences (all) | 20 | 14 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 121 / 371 (32.61%) | 111 / 371 (29.92%) | |
| occurrences (all) | 189 | 171 | |
| Bone pain | | | |
| subjects affected / exposed | 57 / 371 (15.36%) | 58 / 371 (15.63%) | |
| occurrences (all) | 75 | 75 | |
| Back pain | | | |
| subjects affected / exposed | 136 / 371 (36.66%) | 133 / 371 (35.85%) | |
| occurrences (all) | 209 | 214 | |
| Joint swelling | | | |
| subjects affected / exposed | 18 / 371 (4.85%) | 19 / 371 (5.12%) | |
| occurrences (all) | 21 | 19 | |
| Muscle spasms | | | |
| subjects affected / exposed | 83 / 371 (22.37%) | 84 / 371 (22.64%) | |
| occurrences (all) | 112 | 110 | |
| Muscular weakness | | | |
| subjects affected / exposed | 52 / 371 (14.02%) | 45 / 371 (12.13%) | |
| occurrences (all) | 58 | 56 | |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 50 / 371 (13.48%) | 49 / 371 (13.21%) | |
| occurrences (all) | 60 | 66 | |
| Musculoskeletal pain | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 21 / 371 (5.66%) | 28 / 371 (7.55%) | |
| occurrences (all) | 24 | 29 | |
| Myalgia | | | |
| subjects affected / exposed | 17 / 371 (4.58%) | 22 / 371 (5.93%) | |
| occurrences (all) | 18 | 27 | |
| Neck pain | | | |
| subjects affected / exposed | 37 / 371 (9.97%) | 30 / 371 (8.09%) | |
| occurrences (all) | 43 | 37 | |
| Pain in jaw | | | |
| subjects affected / exposed | 12 / 371 (3.23%) | 19 / 371 (5.12%) | |
| occurrences (all) | 12 | 23 | |
| Pain in extremity | | | |
| subjects affected / exposed | 78 / 371 (21.02%) | 76 / 371 (20.49%) | |
| occurrences (all) | 97 | 118 | |
| Spinal pain | | | |
| subjects affected / exposed | 23 / 371 (6.20%) | 15 / 371 (4.04%) | |
| occurrences (all) | 31 | 19 | |
| Infections and infestations | | | |
| Cystitis | | | |
| subjects affected / exposed | 20 / 371 (5.39%) | 13 / 371 (3.50%) | |
| occurrences (all) | 22 | 14 | |
| Cellulitis | | | |
| subjects affected / exposed | 26 / 371 (7.01%) | 21 / 371 (5.66%) | |
| occurrences (all) | 30 | 26 | |
| Bronchitis | | | |
| subjects affected / exposed | 52 / 371 (14.02%) | 46 / 371 (12.40%) | |
| occurrences (all) | 95 | 99 | |
| Influenza | | | |
| subjects affected / exposed | 20 / 371 (5.39%) | 14 / 371 (3.77%) | |
| occurrences (all) | 31 | 18 | |
| Herpes zoster | | | |
| subjects affected / exposed | 18 / 371 (4.85%) | 23 / 371 (6.20%) | |
| occurrences (all) | 19 | 23 | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 62 / 371 (16.71%) | 60 / 371 (16.17%) | |
| occurrences (all) | 129 | 120 | |

| | | | |
|---|---|---|---|
| Oral herpes | | | |
| subjects affected / exposed | 11 / 371 (2.96%) | 23 / 371 (6.20%) | |
| occurrences (all) | 20 | 29 | |
| Pneumonia | | | |
| subjects affected / exposed | 23 / 371 (6.20%) | 33 / 371 (8.89%) | |
| occurrences (all) | 29 | 37 | |
| Sinusitis | | | |
| subjects affected / exposed | 17 / 371 (4.58%) | 23 / 371 (6.20%) | |
| occurrences (all) | 20 | 32 | |
| Respiratory tract infection | | | |
| subjects affected / exposed | 34 / 371 (9.16%) | 38 / 371 (10.24%) | |
| occurrences (all) | 67 | 90 | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 84 / 371 (22.64%) | 82 / 371 (22.10%) | |
| occurrences (all) | 162 | 142 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 56 / 371 (15.09%) | 58 / 371 (15.63%) | |
| occurrences (all) | 111 | 114 | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 86 / 371 (23.18%) | 100 / 371 (26.95%) | |
| occurrences (all) | 113 | 117 | |
| Dehydration | | | |
| subjects affected / exposed | 22 / 371 (5.93%) | 25 / 371 (6.74%) | |
| occurrences (all) | 24 | 29 | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 69 / 371 (18.60%) | 120 / 371 (32.35%) | |
| occurrences (all) | 121 | 255 | |
| Hypoalbuminaemia | | | |
| subjects affected / exposed | 21 / 371 (5.66%) | 24 / 371 (6.47%) | |
| occurrences (all) | 36 | 61 | |
| Hypokalaemia | | | |
| subjects affected / exposed | 91 / 371 (24.53%) | 84 / 371 (22.64%) | |
| occurrences (all) | 183 | 175 | |
| Hypocalcaemia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 75 / 371 (20.22%) | 73 / 371 (19.68%) | |
| occurrences (all) | 169 | 160 | |
| Hypomagnesaemia | | | |
| subjects affected / exposed | 23 / 371 (6.20%) | 41 / 371 (11.05%) | |
| occurrences (all) | 32 | 67 | |
| Hypophosphataemia | | | |
| subjects affected / exposed | 16 / 371 (4.31%) | 20 / 371 (5.39%) | |
| occurrences (all) | 25 | 36 | |
| Hyponatraemia | | | |
| subjects affected / exposed | 17 / 371 (4.58%) | 27 / 371 (7.28%) | |
| occurrences (all) | 20 | 37 | |

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 15 March 2012 | Clarification of subject eligibility or study procedures.<br>Modification of screening requirements to conform to the standard of care and to enhance overall study conduct.<br>A revision was made to timing of when pregnancy testing must be completed. This change is in compliance with a recently approved, company-wide SOP for women of childbearing potential participating in clinical trials conducted by the Sponsor.<br>The inclusion criteria have been revised to clarify that refusal to undergo high dose therapy with SCT is NOT sufficient for entry onto 006 for a subject < 65 years old. There must be a comorbidity that prevents SCT for a subject < 65 years old.<br>Instructions for what should be done with missed doses of lenalidomide or dexamethasone.<br>Revisions are made to exclusion criteria for clarity and consistency throughout the development program.<br>The requirement to discontinue elotuzumab and lenalidomide if a subject becomes pregnant.<br>Timing and details surrounding when certain study assessments are performed.<br>An update to the shelf-life of reconstituted elotuzumab.<br>Correction of typographical errors. |
| 21 May 2014 | Elotuzumab infusion rate escalation plan added to decrease the infusion of elotuzumab to approximately 1 hour<br>Change to the UPEP efficacy testing to reduce the requirement of 24 hour urine collection in a subset of patients<br>Broadening of the medications that can be used for thromboprophylaxis.<br>Additional Clarifications in the protocol serve to reduce any ambiguity regarding study procedures, and provide additional guidance of the EBMT efficacy requirements. |
| 21 August 2014 | Planned Interim Analysis will now take place at 70% of events (338 events) compared to the previous timepoint of 241 (50%) progression events<br>BPI-SF pain severity and pain interference will be evaluated as a secondary endpoint, and formal comparison between treatment arms will be conducted, though it will not be included hierarchical testing.<br>Addition of exploratory objectives to assess PFS at 1, 2 and 3 years and OS rates at 3, 4, 5 and 6 years.<br>Correction of typographical errors in the protocol and appendix documents. |
| 17 August 2015 | Update statistical assumptions and protocol treatment rationale based on currently available published data<br>Clarify requirements for subjects with no measureable urine M protein at baseline<br>Inclusion of new PK/HAHA collection after Cycle 18<br>Inclusion of updated safety information regarding use of adequate contraception based on recent elotuzumab PK data.<br>Change recommended diluent volume of elotuzumab from fixed volumes to range of 100-500 mL. |

| | |
|---|---|
| 24 August 2016 | To promote PFS rates from an exploratory objective to a secondary objective, and to expand the assessment of PFS rates from 1,2,3 years to cover years 1-5, inclusive.<br>Add Time-to-next-treatment (TTNT) as exploratory objective<br>Remove the following sentence from Section 4.3.1. "On the days of elotuzumab administration, the dose of lenalidomide is to be administered at least 2 hours after completion of elotuzumab dosing.<br>Change referencing of Experimental treatment arm of lenalidomide/dexamethasone + elotuzumab from LdE to E-Ld.<br>Add Section 8.3.7-Time to Next Treatment (TTNT)<br>Add Section 9.1.2.1 Source Documentation<br>Update Section 9.2.2 Study Drug Records |

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

None reported