# Clinical trial results:
# A Phase IIIb/IV Safety Trial of Flat Dose Nivolumab in Combination with Ipilimumab in Participants with Non-Small Cell Lung Cancer
# CheckMate 817, CHECKpoint pathway and nivoluMAb clinical Trial Evaluation

## Summary

| | |
|---|---|
| EudraCT number | 2016-002621-10 |
| Trial protocol | HU ES DE NL GR BE GB PL FR CZ IT RO |
| Global end of trial date | 13 May 2022 |

### Results information

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 19 May 2023 |
| First version publication date | 19 May 2023 |

## Trial information

### Trial identification

| | |
|---|---|
| Sponsor protocol code | CA209-817 |

### 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 | Chaussee de la Hulpe 185, Brussels, Belgium, 1170 |
| Public contact | Bristol-Myers Squibb International Corporation, EU Study Start-Up Unit, 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 | 29 July 2022 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 13 May 2022 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

To characterize the safety of Nivolumab flat dosing in combination with weight-based Ipilimumab administration in participants with Non-Small Cell Lung Cancer (NSCLC)

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 participants were followed.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 05 October 2016 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Belgium: 37 |
| Country: Number of subjects enrolled | Canada: 54 |
| Country: Number of subjects enrolled | France: 92 |
| Country: Number of subjects enrolled | Germany: 46 |
| Country: Number of subjects enrolled | Greece: 23 |
| Country: Number of subjects enrolled | Hungary: 23 |
| Country: Number of subjects enrolled | Italy: 76 |
| Country: Number of subjects enrolled | Netherlands: 13 |
| Country: Number of subjects enrolled | Poland: 53 |
| Country: Number of subjects enrolled | Russian Federation: 25 |
| Country: Number of subjects enrolled | Spain: 146 |
| Country: Number of subjects enrolled | Switzerland: 23 |
| Country: Number of subjects enrolled | United Kingdom: 45 |
| Country: Number of subjects enrolled | United States: 229 |
| Country: Number of subjects enrolled | Argentina: 21 |
| Country: Number of subjects enrolled | Brazil: 11 |
| Country: Number of subjects enrolled | Chile: 28 |
| Country: Number of subjects enrolled | Mexico: 4 |
| Country: Number of subjects enrolled | Romania: 75 |
| Country: Number of subjects enrolled | Czechia: 11 |

| | |
|---|---|
| Country: Number of subjects enrolled | Turkey: 6 |
| Worldwide total number of subjects | 1041 |
| EEA total number of subjects | 595 |

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) | 488 |
| From 65 to 84 years | 546 |
| 85 years and over | 7 |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Analysis for the NSCLC special population cohort A1 is pre-specified as exploratory.

### Period 1

| | |
|---|---|
| Period 1 title | Overall Study (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Non-randomised - controlled |
| Blinding used | Not blinded |

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Cohort A |

Arm description:

First-line NSCLC: Nivolumab 240 mg IV Q2W + Ipilimumab 1 mg/kg IV Q6W, starting on Day 1, until progression, unacceptable toxicity, withdrawal of consent, 24 months of treatment from the first dose, or the study ends, whichever occurs first

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Ipilimumab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

1 mg/kg Q6W

| | |
|---|---|
| Investigational medicinal product name | Nivolumab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

240 mg Q2W

| | |
|---|---|
| **Arm title** | Cohort A1 |

Arm description:

First-line NSCLC special population: Nivolumab 240 mg IV Q2W + Ipilimumab 1 mg/kg IV Q6W, starting on Day 1, until progression, unacceptable toxicity, withdrawal of consent, 24 months of treatment from the first dose, or the study ends, whichever occurs first

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Ipilimumab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

1 mg/kg Q6W

| | |
|---|---|
| Investigational medicinal product name | Nivolumab |
| Investigational medicinal product code | |
| Other name | |

| | |
|---|---|
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

240 mg Q2W

| **Arm title** | Cohort B |
|---|---|

Arm description:

Second-line NSCLC: Nivolumab 240 mg IV Q2W + Ipilimumab 1 mg/kg IV Q6W, starting on Day 1, until progression, unacceptable toxicity, withdrawal of consent, 24 months of treatment from the first dose, or the study ends, whichever occurs first

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Ipilimumab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

1 mg/kg Q6W

| | |
|---|---|
| Investigational medicinal product name | Nivolumab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

240 mg Q2W

| **Arm title** | Cohort C |
|---|---|

Arm description:

First-line NSCLC high tumor mutational burden (H-TMB >= 10 mutations/MB): Nivolumab 240 mg IV Q2W + Ipilimumab 1 mg/kg IV Q6W, starting on Day 1, until progression, unacceptable toxicity, withdrawal of consent, 24 months of treatment from the first dose, or the study ends, whichever occurs first

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Ipilimumab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

1 mg/kg Q6W

| | |
|---|---|
| Investigational medicinal product name | Nivolumab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

240 mg Q2W

| **Number of subjects in period 1** | Cohort A | Cohort A1 | Cohort B |
|---|---|---|---|
| Started | 391 | 198 | 395 |
| Completed | 56 | 16 | 30 |
| Not completed | 335 | 182 | 365 |
| Adverse event, serious fatal | 7 | 3 | 5 |
| Consent withdrawn by subject | 5 | 2 | 7 |
| Disease progression | 184 | 109 | 260 |
| Adverse Event unrelated to study drug | 30 | 18 | 21 |
| Study drug toxicity | 90 | 32 | 55 |
| Maximum clinical benefit | 5 | 2 | 1 |
| Participant no longer meets study criteria | - | 1 | 1 |
| Other reasons | 4 | 8 | 6 |
| Poor/Non-compliance | - | 2 | 1 |
| Lost to follow-up | - | - | 2 |
| Participant request to discontinue study treatment | 10 | 5 | 5 |
| Administrative reason by sponsor | - | - | 1 |

| **Number of subjects in period 1** | Cohort C |
|---|---|
| Started | 57 |
| Completed | 12 |
| Not completed | 45 |
| Adverse event, serious fatal | 1 |
| Consent withdrawn by subject | 2 |
| Disease progression | 19 |
| Adverse Event unrelated to study drug | 6 |
| Study drug toxicity | 14 |
| Maximum clinical benefit | - |
| Participant no longer meets study criteria | - |
| Other reasons | - |
| Poor/Non-compliance | - |
| Lost to follow-up | - |
| Participant request to discontinue study treatment | 3 |
| Administrative reason by sponsor | - |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Cohort A |
| Reporting group description: | |
| First-line NSCLC: Nivolumab 240 mg IV Q2W + Ipilimumab 1 mg/kg IV Q6W, starting on Day 1, until progression, unacceptable toxicity, withdrawal of consent, 24 months of treatment from the first dose, or the study ends, whichever occurs first | |
| Reporting group title | Cohort A1 |
| Reporting group description: | |
| First-line NSCLC special population: Nivolumab 240 mg IV Q2W + Ipilimumab 1 mg/kg IV Q6W, starting on Day 1, until progression, unacceptable toxicity, withdrawal of consent, 24 months of treatment from the first dose, or the study ends, whichever occurs first | |
| Reporting group title | Cohort B |
| Reporting group description: | |
| Second-line NSCLC: Nivolumab 240 mg IV Q2W + Ipilimumab 1 mg/kg IV Q6W, starting on Day 1, until progression, unacceptable toxicity, withdrawal of consent, 24 months of treatment from the first dose, or the study ends, whichever occurs first | |
| Reporting group title | Cohort C |
| Reporting group description: | |
| First-line NSCLC high tumor mutational burden (H-TMB >= 10 mutations/MB): Nivolumab 240 mg IV Q2W + Ipilimumab 1 mg/kg IV Q6W, starting on Day 1, until progression, unacceptable toxicity, withdrawal of consent, 24 months of treatment from the first dose, or the study ends, whichever occurs first | |

| Reporting group values | Cohort A | Cohort A1 | Cohort B |
|---|---|---|---|
| Number of subjects | 391 | 198 | 395 |
| Age Categorical<br>Units: Participants | | | |
| < 65 years old | 183 | 81 | 200 |
| >= 65 and < 85 years old | 206 | 115 | 195 |
| >= 85 years old | 2 | 2 | 0 |
| Sex: Female, Male<br>Units: Participants | | | |
| Female | 155 | 71 | 128 |
| Male | 236 | 127 | 267 |
| Race (NIH/OMB)<br>Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | 0 |
| Asian | 3 | 0 | 4 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 |
| Black or African American | 6 | 3 | 5 |
| White | 379 | 194 | 382 |
| More than one race | 0 | 0 | 0 |
| Unknown or Not Reported | 3 | 1 | 4 |
| Ethnicity (NIH/OMB)<br>Units: Subjects | | | |
| Hispanic or Latino | 10 | 13 | 12 |
| Not Hispanic or Latino | 185 | 78 | 175 |
| Unknown or Not Reported | 196 | 107 | 208 |

| **Reporting group values** | Cohort C | Total | |
|---|---|---|---|
| Number of subjects | 57 | 1041 | |
| Age Categorical<br>Units: Participants | | | |
| < 65 years old | 24 | 488 | |
| >= 65 and < 85 years old | 30 | 546 | |
| >= 85 years old | 3 | 7 | |
| Sex: Female, Male<br>Units: Participants | | | |
| Female | 29 | 383 | |
| Male | 28 | 658 | |
| Race (NIH/OMB)<br>Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | |
| Asian | 0 | 7 | |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | |
| Black or African American | 8 | 22 | |
| White | 47 | 1002 | |
| More than one race | 0 | 0 | |
| Unknown or Not Reported | 2 | 10 | |
| Ethnicity (NIH/OMB)<br>Units: Subjects | | | |
| Hispanic or Latino | 3 | 38 | |
| Not Hispanic or Latino | 54 | 492 | |
| Unknown or Not Reported | 0 | 511 | |

## End points

### End points reporting groups

| Reporting group title | Cohort A |
|---|---|
| Reporting group description: | |
| First-line NSCLC: Nivolumab 240 mg IV Q2W + Ipilimumab 1 mg/kg IV Q6W, starting on Day 1, until progression, unacceptable toxicity, withdrawal of consent, 24 months of treatment from the first dose, or the study ends, whichever occurs first | |
| Reporting group title | Cohort A1 |
| Reporting group description: | |
| First-line NSCLC special population: Nivolumab 240 mg IV Q2W + Ipilimumab 1 mg/kg IV Q6W, starting on Day 1, until progression, unacceptable toxicity, withdrawal of consent, 24 months of treatment from the first dose, or the study ends, whichever occurs first | |
| Reporting group title | Cohort B |
| Reporting group description: | |
| Second-line NSCLC: Nivolumab 240 mg IV Q2W + Ipilimumab 1 mg/kg IV Q6W, starting on Day 1, until progression, unacceptable toxicity, withdrawal of consent, 24 months of treatment from the first dose, or the study ends, whichever occurs first | |
| Reporting group title | Cohort C |
| Reporting group description: | |
| First-line NSCLC high tumor mutational burden (H-TMB >= 10 mutations/MB): Nivolumab 240 mg IV Q2W + Ipilimumab 1 mg/kg IV Q6W, starting on Day 1, until progression, unacceptable toxicity, withdrawal of consent, 24 months of treatment from the first dose, or the study ends, whichever occurs first | |

### Primary: Number of Participants with High Grade (Grade 3-4 and Grade 5) Drug-Related Select Adverse Events (AEs)

| End point title | Number of Participants with High Grade (Grade 3-4 and Grade 5) Drug-Related Select Adverse Events (AEs)[1][2] |
|---|---|
| End point description: | |
| Drug related AEs are those events with relationship to study drug. If the relationship to study drug is missing, the AE will be considered as drug-related. The select AEs of interest are the following: Pulmonary, Renal, Gastrointestinal, Hepatic, Skin, Endocrine, and hypersensitivity/infusion reaction events. AEs are reported using the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) version 4.<br>Grade 3= Prolonged severe reaction<br>Grade 4= Life threatening<br>Grade 5= Death | |
| End point type | Primary |
| End point timeframe: | |
| From first dose to 30 days post last dose (Up to approximately 27 months) | |

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only summary statistics planned for this endpoint.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only pre-specified arms planned for this endpoint.

| End point values | Cohort A | Cohort B | Cohort C | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 391 | 395 | 57 | |
| Units: Participants | | | | |
| Gastrointestinal AEs grade 3-4 | 19 | 15 | 4 | |
| Gastrointestinal AEs grade 5 | 0 | 0 | 0 | |
| Hepatic AEs grade 3-4 | 25 | 17 | 3 | |
| Hepatic AEs grade 5 | 0 | 0 | 0 | |
| Pulmonary AEs grade 3-4 | 18 | 11 | 2 | |
| Pulmonary AEs grade 5 | 0 | 1 | 0 | |
| Renal AEs grade 3-4 | 2 | 1 | 1 | |
| Renal AEs grade 5 | 0 | 0 | 0 | |
| Skin AEs grade 3-4 | 14 | 9 | 2 | |
| Skin AEs grade 5 | 0 | 0 | 0 | |
| Endocrine AEs grade 3-4 | 18 | 11 | 2 | |
| Endocrine AEs grade 5 | 0 | 0 | 0 | |
| Hypersensitivity/Infusion Reaction grade 3-4 | 6 | 3 | 0 | |
| Hypersensitivity/Infusion Reaction grade 5 | 0 | 0 | 0 | |

## Statistical analyses

No statistical analyses for this end point

## Primary: Number of Participants with High Grade (Grade 3-4 and Grade 5) Immune-Mediated Adverse Events (imAEs)

| End point title | Number of Participants with High Grade (Grade 3-4 and Grade 5) Immune-Mediated Adverse Events (imAEs)[3][4] |
|---|---|

End point description:

imAEs are specific events that include pneumonitis, diarrhea/colitis, hepatitis, nephritis/renal dysfunction, rash, and endocrine (adrenal insufficiency, hypothyroidism/thyroiditis, hyperthyroidism, diabetes mellitus, and hypophysitis). AEs are reported using the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) version 4.
Grade 3= Prolonged severe reaction
Grade 4= Life threatening
Grade 5= Death

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

End point timeframe:

From first dose to 100 days post last dose (Up to approximately 29 months)

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only summary statistics planned for this endpoint.

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only pre-specified arms planned for this endpoint.

| End point values | Cohort A | Cohort B | Cohort C | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 391 | 395 | 57 | |
| Units: Participants | | | | |
| Pneumonitis grade 3-4 | 20 | 14 | 3 | |
| Diarrhea/Colitis grade 3-4 | 19 | 15 | 3 | |
| Hepatitis grade 3-4 | 18 | 13 | 1 | |
| Adrenal Insufficiency grade 3-4 | 5 | 4 | 1 | |
| Hypothyroidism/Thyroiditis grade 3-4 | 2 | 2 | 0 | |
| Hypothyroidism grade 3-4 | 1 | 1 | 0 | |
| Thyroiditis grade 3-4 | 1 | 1 | 0 | |
| Diabetes Mellitus grade 3-4 | 1 | 0 | 0 | |
| Nephritis and Renal Dysfunction grade 3-4 | 2 | 1 | 0 | |
| Rash grade 3-4 | 14 | 8 | 1 | |
| Hypersensitivity grade 3-4 | 4 | 2 | 0 | |
| Hyperthyroidism grade 3-4 | 0 | 2 | 0 | |
| Hypophysitis grade 3-4 | 3 | 1 | 1 | |
| Any category imAEs grade 5 | 0 | 0 | 0 | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Progression Free Survival (PFS)

| End point title | Progression Free Survival (PFS)[5] |
|---|---|

End point description:

PFS is defined as the time from first dosing date to the date of the first documented tumor progression, as determined by investigators (per RECIST v1.1), or death due to any cause, whichever occurs first. Progressive Disease (PD)= ≥ 20% increase in the sum of the diameters of target lesions, taking as reference the smallest sum on study. The sum must also demonstrate an absolute increase of ≥ 5 mm. The appearance of one or more new lesions is also considered progression.

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

End point timeframe:

From first dosing date to the date of first documented tumor progression or, death due to any cause, whichever occurs first (Up to approximately 67 months)

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only pre-specified arms planned for this endpoint.

| End point values | Cohort A | Cohort B | Cohort C | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 391 | 395 | 57 | |
| Units: Months | | | | |
| median (confidence interval 95%) | 5.75 (4.50 to 7.62) | 3.91 (2.89 to 4.24) | 11.10 (6.47 to 18.40) | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Duration of Response (DoR)

| End point title | Duration of Response (DoR)[6] |
|---|---|

End point description:

DoR is defined as the time between the date of first confirmed complete response (CR) or partial response (PR) to the date of the first documented tumor progression per RECIST 1.1, or death due to any cause, whichever occurs first.
CR= Disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to < 10 mm.
PR= ≥ 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters.
Progressive Disease (PD)= ≥ 20% increase in the sum of the diameters of target lesions, taking as reference the smallest sum on study. The sum must also demonstrate an absolute increase of ≥ 5 mm. The appearance of one or more new lesions is also considered progression.
99999=Not available

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

End point timeframe:

From first dosing date to the date of first documented tumor progression or, death due to any cause, whichever occurs first (Up to approximately 67 months)

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only pre-specified arms planned for this endpoint.

| End point values | Cohort A | Cohort B | Cohort C | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 146 | 90 | 26 | |
| Units: Months | | | | |
| median (confidence interval 95%) | 27.56 (20.40 to 36.04) | 13.01 (10.12 to 19.29) | 26.05 (12.22 to 99999) | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Objective Response Rate (ORR)

| End point title | Objective Response Rate (ORR)[7] |
|---|---|

End point description:

ORR is defined as the percentage of participants with a best overall response of confirmed complete response (CR) or partial response (PR).
CR= Disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to < 10 mm.
PR= ≥ 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters.

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

End point timeframe:

From first dosing date up to approximately 67 months

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only pre-specified arms planned for this endpoint.

| End point values | Cohort A | Cohort B | Cohort C | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 391 | 395 | 57 | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 37.3 (32.5 to 42.3) | 22.8 (18.7 to 27.2) | 45.6 (32.4 to 59.3) | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Overall Survival (OS)

| End point title | Overall Survival (OS)[8] |
|---|---|

End point description:

OS is defined as the time from first dosing date to the date of death. A participant who has not died will be censored at last known date alive.
99999=Not available

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

End point timeframe:

From first dosing date to the date of death (Up to approximately 67 months)

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only pre-specified arms planned for this endpoint.

| End point values | Cohort A | Cohort B | Cohort C | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 391 | 395 | 57 | |
| Units: Months | | | | |
| median (confidence interval 95%) | 16.76 (16.65 to 22.41) | 10.45 (8.84 to 12.22) | 26.09 (21.85 to 99999) | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline in Health-Related Quality of Life (HRQoL) using Functional Assessment of Cancer Therapy-Lung (FACT-L)

| End point title | Change from Baseline in Health-Related Quality of Life (HRQoL) using Functional Assessment of Cancer Therapy-Lung (FACT-L)[9] |
|---|---|

End point description:

FACT-L is a quality-of-life questionnaire which includes the Lung Cancer Subscale (LCS) that assesses the treatment impact on lung cancer related symptoms in 5 domains: Physical, social/family, emotional, and functional well-being using a 5-point scale (0=not at all) to (4=very much) added to obtain total score. The ranges of possible total scores are 0 - 136 for the FACT-L with a higher score representing better quality of life, improved symptomatology and enhanced physical/functional outcomes. According to Functional Assessment of Chronic Illness Therapy scoring guidelines, in the event of missing responses for some of the questions/items, scores will be prorated using the average of the other answers in that scale.
Baseline is defined as evaluations or events that occur before the date and time of the first dose of

study treatment.
Post treatment follow-up includes 2 visits for safety and subsequent survival follow-up every 3 months.
99999=Not available

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

End point timeframe:

From baseline and up to survival follow-up 18 (Up to approximately 67 months)

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only pre-specified arms planned for this endpoint.

| **End point values** | Cohort A | Cohort B | Cohort C | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 364[10] | 365[11] | 57[12] | |
| Units: Units on a Scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline | 94.89 (± 19.33) | 91.20 (± 18.45) | 93.96 (± 17.28) | |
| Week 6 | -0.84 (± 13.82) | -0.30 (± 14.87) | 2.72 (± 12.95) | |
| Survival Follow-up 6 | 14.68 (± 13.58) | 3.81 (± 18.59) | 15.33 (± 37.71) | |
| Survival Follow-up 16 | 5.28 (± 28.19) | -18.00 (± 99999) | 99999 (± 99999) | |
| Survival Follow-up 18 | -43.33 (± 99999) | 99999 (± 99999) | 99999 (± 99999) | |

Notes:

[10] - Baseline= 364
Week 6= 245
Survival Follow-up 6= 22
Survival Follow-up 16= 3
Survival Follow-up 18= 1
[11] - Baseline= 365
Week 6= 244
Survival Follow-up 6=16
Survival Follow-up 16=1
Survival Follow-up 18=0
[12] - Baseline= 57
Week 6= 41
Survival Follow-up 6= 2
Survival Follow-up 16= 0
Survival Follow-up 18= 0

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

SAEs and AEs are assessed from first dose to 100 days post last dose (Up to approximately 29 months). Participants were assessed for deaths (all causes) from their first dose to study completion (Up to approximately 67 months).

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

### Dictionary used

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|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 25.0 |

### Reporting groups

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| Reporting group title | Cohort A |

Reporting group description:

First-line NSCLC: Nivolumab 240 mg IV Q2W + Ipilimumab 1 mg/kg IV Q6W, starting on Day 1, until progression, unacceptable toxicity, withdrawal of consent, 24 months of treatment from the first dose, or the study ends, whichever occurs first

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| Reporting group title | Cohort C |

Reporting group description:

First-line NSCLC high tumor mutational burden (H-TMB >= 10 mutations/MB): Nivolumab 240 mg IV Q2W + Ipilimumab 1 mg/kg IV Q6W, starting on Day 1, until progression, unacceptable toxicity, withdrawal of consent, 24 months of treatment from the first dose, or the study ends, whichever occurs first

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| Reporting group title | Cohort B |

Reporting group description:

Second-line NSCLC: Nivolumab 240 mg IV Q2W + Ipilimumab 1 mg/kg IV Q6W, starting on Day 1, until progression, unacceptable toxicity, withdrawal of consent, 24 months of treatment from the first dose, or the study ends, whichever occurs first

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| Reporting group title | Cohort A1 |

Reporting group description:

First-line NSCLC special population: Nivolumab 240 mg IV Q2W + Ipilimumab 1 mg/kg IV Q6W, starting on Day 1, until progression, unacceptable toxicity, withdrawal of consent, 24 months of treatment from the first dose, or the study ends, whichever occurs first

| **Serious adverse events** | Cohort A | Cohort C | Cohort B |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 264 / 391 (67.52%) | 42 / 57 (73.68%) | 282 / 395 (71.39%) |
| number of deaths (all causes) | 294 | 32 | 334 |
| number of deaths resulting from adverse events | 101 | 15 | 159 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Malignant neoplasm progression | | | |
| subjects affected / exposed | 81 / 391 (20.72%) | 6 / 57 (10.53%) | 144 / 395 (36.46%) |
| occurrences causally related to treatment / all | 0 / 82 | 0 / 6 | 0 / 151 |
| deaths causally related to treatment / all | 0 / 73 | 0 / 4 | 0 / 134 |
| Lymphangiosis carcinomatosa | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colon neoplasm | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cancer pain | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bladder neoplasm | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 2 / 395 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bladder cancer | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tumour pain | | | |
| subjects affected / exposed | 2 / 391 (0.51%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tumour obstruction | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tumour compression | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Transitional cell carcinoma | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 2 / 395 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory tract neoplasm | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pericardial effusion malignant | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neuroma | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metastases to central nervous system | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 2 / 395 (0.51%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metastases to bone | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Malignant pleural effusion | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |
| Brachiocephalic vein thrombosis | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peripheral arterial occlusive disease | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peripheral ischaemia | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Subclavian vein thrombosis | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Superior vena cava syndrome | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 1 / 57 (1.75%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thrombosis | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 2 / 395 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infarction | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypotension | | | |
| subjects affected / exposed | 3 / 391 (0.77%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Exsanguination | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 1 / 57 (1.75%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Embolism | | | |

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|---|---|---|---|
| subjects affected / exposed | 2 / 391 (0.51%) | 0 / 57 (0.00%) | 2 / 395 (0.51%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 3 / 391 (0.77%) | 0 / 57 (0.00%) | 2 / 395 (0.51%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vena cava thrombosis | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Disease progression | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| Death | | | |
| subjects affected / exposed | 2 / 391 (0.51%) | 0 / 57 (0.00%) | 2 / 395 (0.51%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 2 |
| Chills | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chest pain | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Asthenia | | | |
| subjects affected / exposed | 4 / 391 (1.02%) | 1 / 57 (1.75%) | 2 / 395 (0.51%) |
| occurrences causally related to treatment / all | 1 / 4 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fatigue | | | |

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|---|---|---|---|
| subjects affected / exposed | 2 / 391 (0.51%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Multiple organ dysfunction syndrome | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 2 / 391 (0.51%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oedema peripheral | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pain | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 4 / 395 (1.01%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Sudden death | | | |
| subjects affected / exposed | 6 / 391 (1.53%) | 2 / 57 (3.51%) | 4 / 395 (1.01%) |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 2 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 6 | 0 / 2 | 0 / 4 |
| Pyrexia | | | |
| subjects affected / exposed | 5 / 391 (1.28%) | 0 / 57 (0.00%) | 7 / 395 (1.77%) |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 0 | 2 / 8 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Mucosal inflammation | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyperthermia | | | |

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|---|---|---|---|
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General physical health deterioration | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 3 / 395 (0.76%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Performance status decreased | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 3 / 395 (0.76%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Ulcer | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune system disorders | | | |
| Hypersensitivity | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Contrast media allergy | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anaphylactic reaction | | | |
| subjects affected / exposed | 2 / 391 (0.51%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Reproductive system and breast disorders | | | |
| Breast inflammation | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

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|---|---|---|---|
| Pelvic pain | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Breast pain | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 6 / 391 (1.53%) | 1 / 57 (1.75%) | 7 / 395 (1.77%) |
| occurrences causally related to treatment / all | 0 / 9 | 0 / 2 | 1 / 9 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Bronchostenosis | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchospasm | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchial obstruction | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 2 / 395 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Atelectasis | | | |
| subjects affected / exposed | 2 / 391 (0.51%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diaphragmatic paralysis | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

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|---|---|---|---|
| Alveolitis | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Acute respiratory failure | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 2 / 57 (3.51%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Asthma | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune-mediated lung disease | | | |
| subjects affected / exposed | 2 / 391 (0.51%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypoxia | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 1 / 57 (1.75%) | 2 / 395 (0.51%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Hypersensitivity pneumonitis | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemoptysis | | | |
| subjects affected / exposed | 5 / 391 (1.28%) | 1 / 57 (1.75%) | 5 / 395 (1.27%) |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 1 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 2 |
| Dyspnoea | | | |
| subjects affected / exposed | 14 / 391 (3.58%) | 2 / 57 (3.51%) | 22 / 395 (5.57%) |
| occurrences causally related to treatment / all | 1 / 14 | 0 / 2 | 0 / 22 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Interstitial lung disease | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary embolism | | | |
| subjects affected / exposed | 2 / 391 (0.51%) | 1 / 57 (1.75%) | 4 / 395 (1.01%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| Pneumothorax | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 1 / 57 (1.75%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonitis | | | |
| subjects affected / exposed | 23 / 391 (5.88%) | 3 / 57 (5.26%) | 17 / 395 (4.30%) |
| occurrences causally related to treatment / all | 22 / 24 | 3 / 3 | 18 / 18 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | 2 / 2 |
| Pleural effusion | | | |
| subjects affected / exposed | 8 / 391 (2.05%) | 0 / 57 (0.00%) | 4 / 395 (1.01%) |
| occurrences causally related to treatment / all | 0 / 9 | 0 / 0 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Lung disorder | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary haemorrhage | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 2 / 395 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| Pulmonary oedema | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory failure | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 9 / 391 (2.30%) | 2 / 57 (3.51%) | 2 / 395 (0.51%) |
| occurrences causally related to treatment / all | 2 / 9 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 3 | 0 / 1 | 0 / 0 |
| Respiratory distress | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Agitation | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Confusional state | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 2 / 395 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Delirium | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Disorientation | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Mental status changes | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 1 / 57 (1.75%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Schizophrenia | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Product issues | | | |

| | | | |
|---|---|---|---|
| Device loosening | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 1 / 57 (1.75%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Device dislocation | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Investigations | | | |
| Oxygen saturation decreased | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Liver function test increased | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 1 / 57 (1.75%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lipase increased | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| International normalised ratio increased | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Amylase increased | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|---|---|---|
| General physical condition abnormal | | | |
| subjects affected / exposed | 2 / 391 (0.51%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| C-reactive protein increased | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Blood gases abnormal | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood creatinine increased | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Influenza B virus test positive | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Weight decreased | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Troponin increased | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Transaminases increased | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Platelet count decreased | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Infusion related reaction | | | |
| subjects affected / exposed | 4 / 391 (1.02%) | 0 / 57 (0.00%) | 2 / 395 (0.51%) |
| occurrences causally related to treatment / all | 4 / 4 | 0 / 0 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Incision site impaired healing | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Femur fracture | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fall | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 1 / 57 (1.75%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anastomotic stenosis | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Upper limb fracture | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Spinal fracture | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Spinal compression fracture | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Road traffic accident | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rib fracture | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 1 / 57 (1.75%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Recall phenomenon | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Post procedural complication | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Poisoning | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Overdose | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 2 / 395 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lumbar vertebral fracture | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lower limb fracture | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Wound evisceration | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Atrial flutter | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 2 / 57 (3.51%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 2 / 391 (0.51%) | 0 / 57 (0.00%) | 3 / 395 (0.76%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 1 / 3 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Angina unstable | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Arrhythmia | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Arteriosclerosis coronary artery | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Atrial fibrillation | | | |
| subjects affected / exposed | 7 / 391 (1.79%) | 2 / 57 (3.51%) | 2 / 395 (0.51%) |
| occurrences causally related to treatment / all | 1 / 7 | 0 / 2 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Acute coronary syndrome | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac tamponade | | | |
| subjects affected / exposed | 2 / 391 (0.51%) | 1 / 57 (1.75%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac failure congestive | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 1 / 57 (1.75%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac failure | | | |
| subjects affected / exposed | 2 / 391 (0.51%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 1 |
| Cardiac arrest | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardio-respiratory arrest | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Pericardial effusion | | | |
| subjects affected / exposed | 6 / 391 (1.53%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myocarditis | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| Myocardial infarction | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 3 / 391 (0.77%) | 2 / 57 (3.51%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| Intracardiac thrombus | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiopulmonary failure | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiogenic shock | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Pericarditis | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sinus tachycardia | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Supraventricular tachycardia | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| **Nervous system disorders** | | | |
| Aphasia | | | |
| subjects affected / exposed | 2 / 391 (0.51%) | 1 / 57 (1.75%) | 3 / 395 (0.76%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Balance disorder | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebral haemorrhage | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Central nervous system lesion | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Burning sensation | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Brain oedema | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebral ischaemia | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Encephalopathy | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 2 / 57 (3.51%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 2 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Encephalitis autoimmune | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Embolic stroke | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dizziness | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cluster headache | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 3 / 391 (0.77%) | 1 / 57 (1.75%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 1 / 3 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| Epilepsy | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Febrile convulsion | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Loss of consciousness | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ischaemic cerebral infarction | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intracranial pressure increased | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune-mediated encephalitis | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hemiparesis | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hemianopia homonymous | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Headache | | | |
| subjects affected / exposed | 2 / 391 (0.51%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemorrhage intracranial | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Guillain-Barre syndrome | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| Monoparesis | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Optic neuritis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Paraesthesia | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Paresis | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peripheral motor neuropathy | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Somnolence | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Seizure | | | |
| subjects affected / exposed | 2 / 391 (0.51%) | 1 / 57 (1.75%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neurological decompensation | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Myasthenic syndrome | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Motor dysfunction | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyramidal tract syndrome | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Spinal cord compression | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Status epilepticus | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Syncope | | | |
| subjects affected / exposed | 2 / 391 (0.51%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Transient aphasia | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Transient ischaemic attack | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vasogenic cerebral oedema | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vertebrobasilar insufficiency | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 2 / 391 (0.51%) | 2 / 57 (3.51%) | 4 / 395 (1.01%) |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 2 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| Autoimmune anaemia | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Leukocytosis | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 1 / 57 (1.75%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thrombocytopenia | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 2 / 395 (0.51%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Febrile neutropenia | | | |
| subjects affected / exposed | 4 / 391 (1.02%) | 0 / 57 (0.00%) | 3 / 395 (0.76%) |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune thrombocytopenia | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ear and labyrinth disorders | | | |
| Vertigo | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 2 / 395 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Eye disorders | | | |

| | | | |
|---|---|---|---|
| Ophthalmoplegia | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Chronic gastritis | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Barrett's oesophagus | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Autoimmune colitis | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ascites | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal pain | | | |
| subjects affected / exposed | 2 / 391 (0.51%) | 1 / 57 (1.75%) | 2 / 395 (0.51%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| Gastritis | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 1 / 57 (1.75%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastric ulcer | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastric perforation | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 1 / 57 (1.75%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Enterocolitis | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 1 / 57 (1.75%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Enteritis | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dysphagia | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 2 / 395 (0.51%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diverticular perforation | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| Diarrhoea | | | |
| subjects affected / exposed | 7 / 391 (1.79%) | 1 / 57 (1.75%) | 11 / 395 (2.78%) |
| occurrences causally related to treatment / all | 6 / 8 | 1 / 1 | 10 / 11 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diaphragmatic hernia | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 1 / 57 (1.75%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Constipation | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal necrosis | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 1 / 57 (1.75%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Colitis | | | |
| subjects affected / exposed | 5 / 391 (1.28%) | 0 / 57 (0.00%) | 6 / 395 (1.52%) |
| occurrences causally related to treatment / all | 5 / 5 | 0 / 0 | 7 / 7 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intestinal obstruction | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune-mediated enterocolitis | | | |
| subjects affected / exposed | 3 / 391 (0.77%) | 0 / 57 (0.00%) | 5 / 395 (1.27%) |
| occurrences causally related to treatment / all | 6 / 6 | 0 / 0 | 7 / 7 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haematochezia | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal toxicity | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intestinal perforation | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 1 / 57 (1.75%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancreatitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oesophagitis | | | |
| subjects affected / exposed | 2 / 391 (0.51%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 3 / 4 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| Nausea | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Mouth ulceration | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lower gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 1 / 57 (1.75%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Large intestine perforation | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Small intestinal obstruction | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 1 / 57 (1.75%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vomiting | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 3 / 391 (0.77%) | 1 / 57 (1.75%) | 2 / 395 (0.51%) |
| occurrences causally related to treatment / all | 1 / 3 | 0 / 1 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Upper gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Subileus | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| Stomatitis | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Hepatobiliary disorders | | | |
| Hepatic failure | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatic function abnormal | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatic haematoma | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Autoimmune hepatitis | | | |
| subjects affected / exposed | 2 / 391 (0.51%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| Bile duct stenosis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Biliary cirrhosis | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cholangitis | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cholecystitis | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 2 / 395 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cholecystitis acute | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Drug-induced liver injury | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 1 / 57 (1.75%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| Liver injury | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypertransaminasaemia | | | |
| subjects affected / exposed | 2 / 391 (0.51%) | 1 / 57 (1.75%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatotoxicity | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 4 / 391 (1.02%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 4 / 4 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| Hepatitis toxic | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatitis | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Liver disorder | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| Toxic skin eruption | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin necrosis | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin lesion | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rash maculo-papular | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rash | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 2 / 395 (0.51%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pustular psoriasis | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Eosinophilic cellulitis | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dermatitis acneiform | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Chronic kidney disease | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Acute kidney injury | | | |
| subjects affected / exposed | 4 / 391 (1.02%) | 0 / 57 (0.00%) | 8 / 395 (2.03%) |
| occurrences causally related to treatment / all | 2 / 4 | 0 / 0 | 3 / 9 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 2 |
| Urinary tract obstruction | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal failure | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Immune-mediated nephritis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hydronephrosis | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haematuria | | | |
| subjects affected / exposed | 3 / 391 (0.77%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cystitis haemorrhagic | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Endocrine disorders | | | |
| Hypophysitis | | | |
| subjects affected / exposed | 3 / 391 (0.77%) | 1 / 57 (1.75%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 3 / 3 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypopituitarism | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Euthyroid sick syndrome | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Autoimmune thyroiditis | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Adrenocorticotropic hormone deficiency | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Adrenal insufficiency | | | |
| subjects affected / exposed | 6 / 391 (1.53%) | 1 / 57 (1.75%) | 4 / 395 (1.01%) |
| occurrences causally related to treatment / all | 5 / 6 | 1 / 1 | 4 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyperthyroidism | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 3 / 395 (0.76%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 3 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| Thyroiditis | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypothyroidism | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Inappropriate antidiuretic hormone secretion | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lymphocytic hypophysitis | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 2 / 395 (0.51%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Arthritis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 391 (0.00%) | 1 / 57 (1.75%) | 2 / 395 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Back pain | | | |
| subjects affected / exposed | 3 / 391 (0.77%) | 0 / 57 (0.00%) | 2 / 395 (0.51%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bone pain | | | |
| subjects affected / exposed | 2 / 391 (0.51%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Flank pain | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Intervertebral disc degeneration | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Muscular weakness | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteonecrosis of jaw | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myalgia | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neck pain | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteoarthritis | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteolysis | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rhabdomyolysis | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| Spinal pain | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pain in extremity | | | |
| subjects affected / exposed | 2 / 391 (0.51%) | 0 / 57 (0.00%) | 2 / 395 (0.51%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pathological fracture | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 1 / 57 (1.75%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Polymyositis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Abscess | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Clostridium difficile colitis | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 1 / 57 (1.75%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cholecystitis infective | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchopulmonary aspergillosis | | | |
| subjects affected / exposed | 2 / 391 (0.51%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchitis bacterial | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 391 (0.51%) | 0 / 57 (0.00%) | 7 / 395 (1.77%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 7 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bacterial infection | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bacteraemia | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atypical pneumonia | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Arthritis bacterial | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Clostridium difficile infection | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colonic abscess | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| Gastroenteritis | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fungal oesophagitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Escherichia urinary tract infection | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Erysipelas | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cystitis | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Diverticulitis intestinal perforated | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diverticulitis | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diarrhoea infectious | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Device related infection | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Encephalitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| Orchitis | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oral candidiasis | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Lung abscess | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 1 / 57 (1.75%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Liver abscess | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Influenza | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infective spondylitis | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infective exacerbation of chronic obstructive airways disease | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Infectious pleural effusion | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peritonitis | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| Infection | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumococcal sepsis | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumocystis jirovecii pneumonia | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 21 / 391 (5.37%) | 2 / 57 (3.51%) | 26 / 395 (6.58%) |
| occurrences causally related to treatment / all | 1 / 26 | 0 / 2 | 3 / 27 |
| deaths causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 1 |
| Pneumonia aspiration | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 1 / 57 (1.75%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia bacterial | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 391 (0.51%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Post procedural infection | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Pyelonephritis acute | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory tract infection | | | |
| subjects affected / exposed | 7 / 391 (1.79%) | 0 / 57 (0.00%) | 3 / 395 (0.76%) |
| occurrences causally related to treatment / all | 0 / 7 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 1 |
| Sepsis | | | |
| subjects affected / exposed | 7 / 391 (1.79%) | 2 / 57 (3.51%) | 5 / 395 (1.27%) |
| occurrences causally related to treatment / all | 0 / 7 | 0 / 2 | 2 / 5 |
| deaths causally related to treatment / all | 0 / 3 | 0 / 1 | 1 / 2 |
| Septic shock | | | |
| subjects affected / exposed | 5 / 391 (1.28%) | 0 / 57 (0.00%) | 2 / 395 (0.51%) |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| Skin infection | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Staphylococcal infection | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urosepsis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 391 (0.51%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| Urinary tract infection | | | |
| subjects affected / exposed | 2 / 391 (0.51%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Staphylococcal sepsis | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Viral infection | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Hypercalcaemia | | | |
| subjects affected / exposed | 3 / 391 (0.77%) | 0 / 57 (0.00%) | 2 / 395 (0.51%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Failure to thrive | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 1 / 57 (1.75%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diabetic ketoacidosis | | | |
| subjects affected / exposed | 2 / 391 (0.51%) | 1 / 57 (1.75%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 2 / 3 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diabetes mellitus | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 2 / 395 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dehydration | | | |
| subjects affected / exposed | 2 / 391 (0.51%) | 2 / 57 (3.51%) | 2 / 395 (0.51%) |
| occurrences causally related to treatment / all | 0 / 2 | 1 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Decreased appetite | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Acidosis | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyperglycaemia | | | |
| subjects affected / exposed | 4 / 391 (1.02%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 2 / 4 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypoglycaemia | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypokalaemia | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyponatraemia | | | |
| subjects affected / exposed | 4 / 391 (1.02%) | 2 / 57 (3.51%) | 3 / 395 (0.76%) |
| occurrences causally related to treatment / all | 2 / 4 | 0 / 3 | 1 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypophagia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Steroid diabetes | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tumour lysis syndrome | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 1 / 395 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Type 1 diabetes mellitus | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Type 2 diabetes mellitus | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypocalcaemia | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 0 / 57 (0.00%) | 0 / 395 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| **Serious adverse events** | Cohort A1 | | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 149 / 198 (75.25%) | | |
| number of deaths (all causes) | 166 | | |
| number of deaths resulting from adverse events | 85 | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Malignant neoplasm progression | | | |
| subjects affected / exposed | 64 / 198 (32.32%) | | |
| occurrences causally related to treatment / all | 0 / 68 | | |
| deaths causally related to treatment / all | 0 / 63 | | |

| | | | | |
|---|---|---|---|---|
| Lymphangiosis carcinomatosa | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Colon neoplasm | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cancer pain | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Bladder neoplasm | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Bladder cancer | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Tumour pain | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Tumour obstruction | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Tumour compression | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Transitional cell carcinoma | | | | |

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|---|---|---|---|---|
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Respiratory tract neoplasm | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pericardial effusion malignant | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Neuroma | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Metastases to central nervous system | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Metastases to bone | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Malignant pleural effusion | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Vascular disorders | | | | |
| Brachiocephalic vein thrombosis | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Peripheral arterial occlusive disease | | | | |

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|---|---|---|---|---|
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Peripheral ischaemia | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Subclavian vein thrombosis | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Superior vena cava syndrome | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 1 | | | |
| Thrombosis | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Infarction | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hypotension | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Exsanguination | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Embolism | | | | |

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|---|---|---|---|---|
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Deep vein thrombosis | | | | |
| subjects affected / exposed | 2 / 198 (1.01%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Vena cava thrombosis | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| General disorders and administration site conditions | | | | |
| Disease progression | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Death | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Chills | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Chest pain | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Asthenia | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Fatigue | | | | |

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|---|---|---|---|---|
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Multiple organ dysfunction syndrome | | | | |
| subjects affected / exposed | 2 / 198 (1.01%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 2 | | | |
| Non-cardiac chest pain | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Oedema peripheral | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pain | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Sudden death | | | | |
| subjects affected / exposed | 4 / 198 (2.02%) | | | |
| occurrences causally related to treatment / all | 0 / 4 | | | |
| deaths causally related to treatment / all | 0 / 4 | | | |
| Pyrexia | | | | |
| subjects affected / exposed | 8 / 198 (4.04%) | | | |
| occurrences causally related to treatment / all | 5 / 8 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Mucosal inflammation | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hyperthermia | | | | |

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|---|---|---|---|---|
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| General physical health deterioration | | | | |
| subjects affected / exposed | 3 / 198 (1.52%) | | | |
| occurrences causally related to treatment / all | 0 / 3 | | | |
| deaths causally related to treatment / all | 0 / 1 | | | |
| Performance status decreased | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Ulcer | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Immune system disorders | | | | |
| Hypersensitivity | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Contrast media allergy | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Anaphylactic reaction | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Reproductive system and breast disorders | | | | |
| Breast inflammation | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |

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|---|---|---|---|---|
| Pelvic pain | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Breast pain | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Respiratory, thoracic and mediastinal disorders | | | | |
| Chronic obstructive pulmonary disease | | | | |
| subjects affected / exposed | 3 / 198 (1.52%) | | | |
| occurrences causally related to treatment / all | 0 / 4 | | | |
| deaths causally related to treatment / all | 0 / 1 | | | |
| Bronchostenosis | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Bronchospasm | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Bronchial obstruction | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Atelectasis | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Diaphragmatic paralysis | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |

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|---|---|---|---|---|
| Alveolitis | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Acute respiratory failure | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 1 | | | |
| Asthma | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Immune-mediated lung disease | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hypoxia | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hypersensitivity pneumonitis | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Haemoptysis | | | | |
| subjects affected / exposed | 2 / 198 (1.01%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Dyspnoea | | | | |
| subjects affected / exposed | 9 / 198 (4.55%) | | | |
| occurrences causally related to treatment / all | 1 / 10 | | | |
| deaths causally related to treatment / all | 0 / 3 | | | |
| Interstitial lung disease | | | | |

| | | | | |
|---|---|---|---|---|
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 1 / 1 | | | |
| Pulmonary embolism | | | | |
| subjects affected / exposed | 6 / 198 (3.03%) | | | |
| occurrences causally related to treatment / all | 0 / 6 | | | |
| deaths causally related to treatment / all | 0 / 1 | | | |
| Pneumothorax | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pneumonitis | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pleural effusion | | | | |
| subjects affected / exposed | 4 / 198 (2.02%) | | | |
| occurrences causally related to treatment / all | 0 / 4 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Lung disorder | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 1 | | | |
| Pulmonary haemorrhage | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 1 | | | |
| Pulmonary oedema | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Respiratory failure | | | | |

| | | | | |
|---|---|---|---|---|
| subjects affected / exposed | 2 / 198 (1.01%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 1 | | | |
| Respiratory distress | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 1 | | | |
| Psychiatric disorders | | | | |
| Agitation | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Confusional state | | | | |
| subjects affected / exposed | 2 / 198 (1.01%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Delirium | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Disorientation | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Mental status changes | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Schizophrenia | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Product issues | | | | |

| | | | | |
|---|---|---|---|---|
| Device loosening | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Device dislocation | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Investigations | | | | |
| Oxygen saturation decreased | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Neutrophil count decreased | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Liver function test increased | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Lipase increased | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| International normalised ratio increased | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Amylase increased | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |

| | | | | |
|---|---|---|---|---|
| General physical condition abnormal | | | | |
| subjects affected / exposed | 2 / 198 (1.01%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| C-reactive protein increased | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Blood gases abnormal | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Blood creatinine increased | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Influenza B virus test positive | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Weight decreased | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Troponin increased | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Transaminases increased | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Platelet count decreased | | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 198 (0.51%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Injury, poisoning and procedural complications | | | |
| Infusion related reaction | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Incision site impaired healing | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Femur fracture | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Fall | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Anastomotic stenosis | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Upper limb fracture | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Spinal fracture | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Spinal compression fracture | | | |

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|---|---|---|---|---|
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Road traffic accident | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Rib fracture | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Recall phenomenon | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Post procedural complication | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Poisoning | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Overdose | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Lumbar vertebral fracture | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Lower limb fracture | | | | |

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|---|---|---|---|---|
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Wound evisceration | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cardiac disorders | | | | |
| Atrial flutter | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Acute myocardial infarction | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Angina unstable | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Arrhythmia | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Arteriosclerosis coronary artery | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Atrial fibrillation | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Acute coronary syndrome | | | | |

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|---|---|---|---|---|
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cardiac tamponade | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cardiac failure congestive | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cardiac failure | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 1 | | | |
| Cardiac arrest | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 1 | | | |
| Cardio-respiratory arrest | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 1 | | | |
| Pericardial effusion | | | | |
| subjects affected / exposed | 2 / 198 (1.01%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Myocarditis | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Myocardial infarction | | | | |

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|---|---|---|---|---|
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Intracardiac thrombus | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cardiopulmonary failure | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cardiogenic shock | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pericarditis | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Sinus tachycardia | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Supraventricular tachycardia | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Nervous system disorders | | | | |
| Aphasia | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Balance disorder | | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cerebral haemorrhage | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Central nervous system lesion | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Burning sensation | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Brain oedema | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cerebral ischaemia | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Encephalopathy | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Encephalitis autoimmune | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Embolic stroke | | | |

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|---|---|---|---|---|
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Dizziness | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cluster headache | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cerebrovascular accident | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Epilepsy | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Febrile convulsion | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Loss of consciousness | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Ischaemic cerebral infarction | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Intracranial pressure increased | | | | |

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|---|---|---|---|---|
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Immune-mediated encephalitis | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hemiparesis | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hemianopia homonymous | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Headache | | | | |
| subjects affected / exposed | 3 / 198 (1.52%) | | | |
| occurrences causally related to treatment / all | 0 / 3 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Haemorrhage intracranial | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Guillain-Barre syndrome | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Monoparesis | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Optic neuritis | | | | |

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|---|---|---|---|---|
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Paraesthesia | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Paresis | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Peripheral motor neuropathy | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Somnolence | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Seizure | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Neurological decompensation | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Myasthenic syndrome | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 1 / 1 | | | |
| Motor dysfunction | | | | |

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|---|---|---|---|---|
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pyramidal tract syndrome | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Spinal cord compression | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Status epilepticus | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Syncope | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Transient aphasia | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Transient ischaemic attack | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Vasogenic cerebral oedema | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Vertebrobasilar insufficiency | | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 2 / 198 (1.01%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Autoimmune anaemia | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Leukocytosis | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Febrile neutropenia | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Immune thrombocytopenia | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Ear and labyrinth disorders | | | |
| Vertigo | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Eye disorders | | | |

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|---|---|---|---|---|
| Ophthalmoplegia | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastrointestinal disorders | | | | |
| Chronic gastritis | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Barrett's oesophagus | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Autoimmune colitis | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Ascites | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Abdominal pain upper | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Abdominal pain | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastritis | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastric ulcer | | | | |

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|---|---|---|---|---|
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastric perforation | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Enterocolitis | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Enteritis | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Dysphagia | | | | |
| subjects affected / exposed | 3 / 198 (1.52%) | | | |
| occurrences causally related to treatment / all | 0 / 4 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Diverticular perforation | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Diarrhoea | | | | |
| subjects affected / exposed | 4 / 198 (2.02%) | | | |
| occurrences causally related to treatment / all | 3 / 4 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Diaphragmatic hernia | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Constipation | | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal necrosis | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Colitis | | | |
| subjects affected / exposed | 3 / 198 (1.52%) | | |
| occurrences causally related to treatment / all | 3 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Intestinal obstruction | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Immune-mediated enterocolitis | | | |
| subjects affected / exposed | 4 / 198 (2.02%) | | |
| occurrences causally related to treatment / all | 4 / 4 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Haematochezia | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal toxicity | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Intestinal perforation | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pancreatitis | | | |

| | | | | |
|---|---|---|---|---|
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Oesophagitis | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Nausea | | | | |
| subjects affected / exposed | 3 / 198 (1.52%) | | | |
| occurrences causally related to treatment / all | 2 / 6 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Mouth ulceration | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Lower gastrointestinal haemorrhage | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Large intestine perforation | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Rectal haemorrhage | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Small intestinal obstruction | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Vomiting | | | | |

| | | | | |
|---|---|---|---|---|
| subjects affected / exposed | 3 / 198 (1.52%) | | | |
| occurrences causally related to treatment / all | 2 / 4 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Upper gastrointestinal haemorrhage | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 1 | | | |
| Subileus | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Stomatitis | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hepatobiliary disorders | | | | |
| Hepatic failure | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hepatic function abnormal | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hepatic haematoma | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Autoimmune hepatitis | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Bile duct stenosis | | | | |

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|---|---|---|---|---|
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Biliary cirrhosis | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 1 | | | |
| Cholangitis | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cholecystitis | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cholecystitis acute | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Drug-induced liver injury | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Liver injury | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hypertransaminasaemia | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hepatotoxicity | | | | |

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|---|---|---|---|---|
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hepatitis toxic | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hepatitis | | | | |
| subjects affected / exposed | 2 / 198 (1.01%) | | | |
| occurrences causally related to treatment / all | 1 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Liver disorder | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Skin and subcutaneous tissue disorders | | | | |
| Toxic skin eruption | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Skin necrosis | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Skin lesion | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Rash maculo-papular | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Rash | | | | |

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|---|---|---|---|---|
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pustular psoriasis | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Eosinophilic cellulitis | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Dermatitis acneiform | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| **Renal and urinary disorders** | | | | |
| Chronic kidney disease | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Acute kidney injury | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Urinary tract obstruction | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Renal failure | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Immune-mediated nephritis | | | | |

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|---|---|---|---|---|
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hydronephrosis | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Haematuria | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cystitis haemorrhagic | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Endocrine disorders | | | | |
| Hypophysitis | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hypopituitarism | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Euthyroid sick syndrome | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Autoimmune thyroiditis | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Adrenocorticotropic hormone deficiency | | | | |

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|---|---|---|---|---|
| subjects affected / exposed | 2 / 198 (1.01%) | | | |
| occurrences causally related to treatment / all | 2 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Adrenal insufficiency | | | | |
| subjects affected / exposed | 2 / 198 (1.01%) | | | |
| occurrences causally related to treatment / all | 2 / 2 | | | |
| deaths causally related to treatment / all | 1 / 1 | | | |
| Hyperthyroidism | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Thyroiditis | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hypothyroidism | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Inappropriate antidiuretic hormone secretion | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Lymphocytic hypophysitis | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| **Musculoskeletal and connective tissue disorders** | | | | |
| Arthralgia | | | | |
| subjects affected / exposed | 5 / 198 (2.53%) | | | |
| occurrences causally related to treatment / all | 1 / 5 | | | |
| deaths causally related to treatment / all | 0 / 1 | | | |
| Arthritis | | | | |

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|---|---|---|---|---|
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Back pain | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Bone pain | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Flank pain | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Intervertebral disc degeneration | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Muscular weakness | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Osteonecrosis of jaw | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Myalgia | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Neck pain | | | | |

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|---|---|---|---|---|
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Osteoarthritis | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Osteolysis | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Musculoskeletal chest pain | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Rhabdomyolysis | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Spinal pain | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pain in extremity | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pathological fracture | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Polymyositis | | | | |

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|---|---|---|---|
| subjects affected / exposed | 1 / 198 (0.51%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 1 / 1 | | |
| Infections and infestations | | | |
| Abscess | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Clostridium difficile colitis | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cholecystitis infective | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Bronchopulmonary aspergillosis | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Bronchitis bacterial | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Bronchitis | | | |

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|---|---|---|---|---|
| subjects affected / exposed | 3 / 198 (1.52%) | | | |
| occurrences causally related to treatment / all | 0 / 4 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Bacterial infection | | | | |
| subjects affected / exposed | 2 / 198 (1.01%) | | | |
| occurrences causally related to treatment / all | 1 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Bacteraemia | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Atypical pneumonia | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Arthritis bacterial | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Clostridium difficile infection | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Colonic abscess | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastroenteritis | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Fungal oesophagitis | | | | |

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|---|---|---|---|---|
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Escherichia urinary tract infection | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Erysipelas | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cystitis | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Diverticulitis intestinal perforated | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Diverticulitis | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Diarrhoea infectious | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Device related infection | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Encephalitis | | | | |

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|---|---|---|---|---|
| subjects affected / exposed | 4 / 198 (2.02%) | | | |
| occurrences causally related to treatment / all | 4 / 5 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Orchitis | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Oral candidiasis | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Lung abscess | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Lower respiratory tract infection | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Liver abscess | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Influenza | | | | |
| subjects affected / exposed | 2 / 198 (1.01%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Infective spondylitis | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Infective exacerbation of chronic obstructive airways disease | | | | |

| | | | | |
|---|---|---|---|---|
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Infectious pleural effusion | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Peritonitis | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Infection | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pneumococcal sepsis | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pneumocystis jirovecii pneumonia | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pneumonia | | | | |
| subjects affected / exposed | 6 / 198 (3.03%) | | | |
| occurrences causally related to treatment / all | 0 / 6 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pneumonia aspiration | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pneumonia bacterial | | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Post procedural infection | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pyelonephritis acute | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory tract infection | | | |
| subjects affected / exposed | 4 / 198 (2.02%) | | |
| occurrences causally related to treatment / all | 0 / 4 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Sepsis | | | |
| subjects affected / exposed | 4 / 198 (2.02%) | | |
| occurrences causally related to treatment / all | 0 / 4 | | |
| deaths causally related to treatment / all | 0 / 4 | | |
| Septic shock | | | |
| subjects affected / exposed | 2 / 198 (1.01%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 2 | | |
| Skin infection | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Staphylococcal infection | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Urosepsis | | | |

| | | | | |
|---|---|---|---|---|
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Urinary tract infection | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Upper respiratory tract infection | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Staphylococcal sepsis | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Viral infection | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Metabolism and nutrition disorders | | | | |
| Hypercalcaemia | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Failure to thrive | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Diabetic ketoacidosis | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Diabetes mellitus | | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Dehydration | | | |
| subjects affected / exposed | 2 / 198 (1.01%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Decreased appetite | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Acidosis | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 3 / 198 (1.52%) | | |
| occurrences causally related to treatment / all | 1 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypoglycaemia | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypokalaemia | | | |
| subjects affected / exposed | 3 / 198 (1.52%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hyponatraemia | | | |
| subjects affected / exposed | 2 / 198 (1.01%) | | |
| occurrences causally related to treatment / all | 1 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypophagia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Steroid diabetes | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Tumour lysis syndrome | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Type 1 diabetes mellitus | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Type 2 diabetes mellitus | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypocalcaemia | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| **Non-serious adverse events** | Cohort A | Cohort C | Cohort B |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 362 / 391 (92.58%) | 56 / 57 (98.25%) | 346 / 395 (87.59%) |
| Vascular disorders | | | |
| Hypotension | | | |
| subjects affected / exposed | 20 / 391 (5.12%) | 7 / 57 (12.28%) | 12 / 395 (3.04%) |
| occurrences (all) | 23 | 7 | 12 |
| General disorders and administration site conditions | | | |

| | | | |
|---|---|---|---|
| Pyrexia | | | |
| subjects affected / exposed | 66 / 391 (16.88%) | 7 / 57 (12.28%) | 51 / 395 (12.91%) |
| occurrences (all) | 96 | 8 | 66 |
| Pain | | | |
| subjects affected / exposed | 20 / 391 (5.12%) | 5 / 57 (8.77%) | 10 / 395 (2.53%) |
| occurrences (all) | 21 | 5 | 11 |
| Oedema peripheral | | | |
| subjects affected / exposed | 39 / 391 (9.97%) | 9 / 57 (15.79%) | 32 / 395 (8.10%) |
| occurrences (all) | 47 | 9 | 36 |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 11 / 391 (2.81%) | 5 / 57 (8.77%) | 11 / 395 (2.78%) |
| occurrences (all) | 13 | 5 | 11 |
| Malaise | | | |
| subjects affected / exposed | 7 / 391 (1.79%) | 3 / 57 (5.26%) | 3 / 395 (0.76%) |
| occurrences (all) | 7 | 3 | 3 |
| Localised oedema | | | |
| subjects affected / exposed | 0 / 391 (0.00%) | 4 / 57 (7.02%) | 0 / 395 (0.00%) |
| occurrences (all) | 0 | 5 | 0 |
| Fatigue | | | |
| subjects affected / exposed | 140 / 391 (35.81%) | 24 / 57 (42.11%) | 87 / 395 (22.03%) |
| occurrences (all) | 170 | 31 | 109 |
| Chills | | | |
| subjects affected / exposed | 16 / 391 (4.09%) | 5 / 57 (8.77%) | 10 / 395 (2.53%) |
| occurrences (all) | 16 | 7 | 10 |
| Asthenia | | | |
| subjects affected / exposed | 84 / 391 (21.48%) | 4 / 57 (7.02%) | 67 / 395 (16.96%) |
| occurrences (all) | 104 | 6 | 83 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Productive cough | | | |
| subjects affected / exposed | 31 / 391 (7.93%) | 6 / 57 (10.53%) | 28 / 395 (7.09%) |
| occurrences (all) | 37 | 6 | 30 |
| Pneumonitis | | | |
| subjects affected / exposed | 31 / 391 (7.93%) | 4 / 57 (7.02%) | 18 / 395 (4.56%) |
| occurrences (all) | 34 | 5 | 21 |
| Hypoxia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 7 / 391 (1.79%) | 8 / 57 (14.04%) | 10 / 395 (2.53%) |
| occurrences (all) | 10 | 8 | 11 |
| Haemoptysis | | | |
| subjects affected / exposed | 20 / 391 (5.12%) | 2 / 57 (3.51%) | 21 / 395 (5.32%) |
| occurrences (all) | 24 | 2 | 24 |
| Dyspnoea | | | |
| subjects affected / exposed | 85 / 391 (21.74%) | 24 / 57 (42.11%) | 85 / 395 (21.52%) |
| occurrences (all) | 97 | 29 | 93 |
| Cough | | | |
| subjects affected / exposed | 98 / 391 (25.06%) | 13 / 57 (22.81%) | 71 / 395 (17.97%) |
| occurrences (all) | 118 | 14 | 82 |
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 7 / 391 (1.79%) | 4 / 57 (7.02%) | 8 / 395 (2.03%) |
| occurrences (all) | 9 | 5 | 9 |
| Nasal congestion | | | |
| subjects affected / exposed | 8 / 391 (2.05%) | 3 / 57 (5.26%) | 5 / 395 (1.27%) |
| occurrences (all) | 9 | 3 | 8 |
| Psychiatric disorders | | | |
| Insomnia | | | |
| subjects affected / exposed | 34 / 391 (8.70%) | 8 / 57 (14.04%) | 17 / 395 (4.30%) |
| occurrences (all) | 38 | 8 | 17 |
| Depression | | | |
| subjects affected / exposed | 21 / 391 (5.37%) | 8 / 57 (14.04%) | 6 / 395 (1.52%) |
| occurrences (all) | 24 | 9 | 6 |
| Anxiety | | | |
| subjects affected / exposed | 19 / 391 (4.86%) | 10 / 57 (17.54%) | 11 / 395 (2.78%) |
| occurrences (all) | 21 | 13 | 11 |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 20 / 391 (5.12%) | 6 / 57 (10.53%) | 19 / 395 (4.81%) |
| occurrences (all) | 27 | 7 | 27 |
| Amylase increased | | | |
| subjects affected / exposed | 27 / 391 (6.91%) | 3 / 57 (5.26%) | 31 / 395 (7.85%) |
| occurrences (all) | 45 | 4 | 61 |
| Aspartate aminotransferase increased | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 14 / 391 (3.58%) | 6 / 57 (10.53%) | 18 / 395 (4.56%) |
| occurrences (all) | 19 | 7 | 26 |
| Blood alkaline phosphatase increased | | | |
| subjects affected / exposed | 10 / 391 (2.56%) | 6 / 57 (10.53%) | 20 / 395 (5.06%) |
| occurrences (all) | 11 | 6 | 30 |
| Blood creatinine increased | | | |
| subjects affected / exposed | 18 / 391 (4.60%) | 8 / 57 (14.04%) | 22 / 395 (5.57%) |
| occurrences (all) | 24 | 9 | 28 |
| Lipase increased | | | |
| subjects affected / exposed | 35 / 391 (8.95%) | 3 / 57 (5.26%) | 31 / 395 (7.85%) |
| occurrences (all) | 51 | 5 | 62 |
| Lymphocyte count decreased | | | |
| subjects affected / exposed | 3 / 391 (0.77%) | 3 / 57 (5.26%) | 2 / 395 (0.51%) |
| occurrences (all) | 3 | 6 | 5 |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 3 / 391 (0.77%) | 3 / 57 (5.26%) | 4 / 395 (1.01%) |
| occurrences (all) | 3 | 4 | 8 |
| Weight decreased | | | |
| subjects affected / exposed | 33 / 391 (8.44%) | 8 / 57 (14.04%) | 23 / 395 (5.82%) |
| occurrences (all) | 35 | 9 | 23 |
| Weight increased | | | |
| subjects affected / exposed | 4 / 391 (1.02%) | 5 / 57 (8.77%) | 5 / 395 (1.27%) |
| occurrences (all) | 4 | 5 | 5 |
| Injury, poisoning and procedural complications | | | |
| Fall | | | |
| subjects affected / exposed | 12 / 391 (3.07%) | 8 / 57 (14.04%) | 8 / 395 (2.03%) |
| occurrences (all) | 12 | 8 | 9 |
| Infusion related reaction | | | |
| subjects affected / exposed | 22 / 391 (5.63%) | 4 / 57 (7.02%) | 11 / 395 (2.78%) |
| occurrences (all) | 26 | 5 | 12 |
| Cardiac disorders | | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 13 / 391 (3.32%) | 3 / 57 (5.26%) | 8 / 395 (2.03%) |
| occurrences (all) | 13 | 3 | 8 |
| Nervous system disorders | | | |

| | | | |
|---|---|---|---|
| Peripheral sensory neuropathy | | | |
| subjects affected / exposed | 2 / 391 (0.51%) | 4 / 57 (7.02%) | 2 / 395 (0.51%) |
| occurrences (all) | 2 | 6 | 2 |
| Headache | | | |
| subjects affected / exposed | 54 / 391 (13.81%) | 10 / 57 (17.54%) | 34 / 395 (8.61%) |
| occurrences (all) | 63 | 17 | 39 |
| Dizziness | | | |
| subjects affected / exposed | 32 / 391 (8.18%) | 7 / 57 (12.28%) | 24 / 395 (6.08%) |
| occurrences (all) | 39 | 7 | 24 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 53 / 391 (13.55%) | 13 / 57 (22.81%) | 53 / 395 (13.42%) |
| occurrences (all) | 65 | 15 | 69 |
| Eye disorders | | | |
| Vision blurred | | | |
| subjects affected / exposed | 10 / 391 (2.56%) | 3 / 57 (5.26%) | 5 / 395 (1.27%) |
| occurrences (all) | 11 | 3 | 5 |
| Dry eye | | | |
| subjects affected / exposed | 7 / 391 (1.79%) | 4 / 57 (7.02%) | 4 / 395 (1.01%) |
| occurrences (all) | 9 | 4 | 4 |
| Gastrointestinal disorders | | | |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 13 / 391 (3.32%) | 4 / 57 (7.02%) | 3 / 395 (0.76%) |
| occurrences (all) | 15 | 6 | 3 |
| Dysphagia | | | |
| subjects affected / exposed | 12 / 391 (3.07%) | 3 / 57 (5.26%) | 11 / 395 (2.78%) |
| occurrences (all) | 12 | 3 | 12 |
| Dry mouth | | | |
| subjects affected / exposed | 20 / 391 (5.12%) | 3 / 57 (5.26%) | 12 / 395 (3.04%) |
| occurrences (all) | 20 | 3 | 12 |
| Diarrhoea | | | |
| subjects affected / exposed | 122 / 391 (31.20%) | 23 / 57 (40.35%) | 80 / 395 (20.25%) |
| occurrences (all) | 217 | 39 | 118 |
| Constipation | | | |
| subjects affected / exposed | 69 / 391 (17.65%) | 11 / 57 (19.30%) | 53 / 395 (13.42%) |
| occurrences (all) | 81 | 12 | 60 |
| Colitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 9 / 391 (2.30%) | 4 / 57 (7.02%) | 3 / 395 (0.76%) |
| occurrences (all) | 9 | 4 | 4 |
| Abdominal pain | | | |
| subjects affected / exposed | 33 / 391 (8.44%) | 7 / 57 (12.28%) | 21 / 395 (5.32%) |
| occurrences (all) | 40 | 11 | 26 |
| Nausea | | | |
| subjects affected / exposed | 97 / 391 (24.81%) | 25 / 57 (43.86%) | 65 / 395 (16.46%) |
| occurrences (all) | 124 | 34 | 80 |
| Vomiting | | | |
| subjects affected / exposed | 63 / 391 (16.11%) | 11 / 57 (19.30%) | 52 / 395 (13.16%) |
| occurrences (all) | 94 | 16 | 61 |
| Oral pain | | | |
| subjects affected / exposed | 1 / 391 (0.26%) | 3 / 57 (5.26%) | 0 / 395 (0.00%) |
| occurrences (all) | 1 | 3 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| Rash | | | |
| subjects affected / exposed | 59 / 391 (15.09%) | 5 / 57 (8.77%) | 52 / 395 (13.16%) |
| occurrences (all) | 81 | 9 | 73 |
| Pruritus | | | |
| subjects affected / exposed | 82 / 391 (20.97%) | 16 / 57 (28.07%) | 79 / 395 (20.00%) |
| occurrences (all) | 123 | 22 | 103 |
| Erythema | | | |
| subjects affected / exposed | 10 / 391 (2.56%) | 0 / 57 (0.00%) | 20 / 395 (5.06%) |
| occurrences (all) | 12 | 0 | 25 |
| Dry skin | | | |
| subjects affected / exposed | 29 / 391 (7.42%) | 2 / 57 (3.51%) | 24 / 395 (6.08%) |
| occurrences (all) | 30 | 2 | 27 |
| Rash maculo-papular | | | |
| subjects affected / exposed | 30 / 391 (7.67%) | 10 / 57 (17.54%) | 16 / 395 (4.05%) |
| occurrences (all) | 39 | 14 | 22 |
| Endocrine disorders | | | |
| Hypothyroidism | | | |
| subjects affected / exposed | 55 / 391 (14.07%) | 12 / 57 (21.05%) | 45 / 395 (11.39%) |
| occurrences (all) | 60 | 13 | 50 |
| Hyperthyroidism | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 31 / 391 (7.93%) | 5 / 57 (8.77%) | 35 / 395 (8.86%) |
| occurrences (all) | 33 | 5 | 38 |
| Adrenal insufficiency | | | |
| subjects affected / exposed | 9 / 391 (2.30%) | 4 / 57 (7.02%) | 7 / 395 (1.77%) |
| occurrences (all) | 9 | 4 | 7 |
| Musculoskeletal and connective tissue disorders | | | |
| Pain in extremity | | | |
| subjects affected / exposed | 30 / 391 (7.67%) | 9 / 57 (15.79%) | 27 / 395 (6.84%) |
| occurrences (all) | 31 | 9 | 30 |
| Myalgia | | | |
| subjects affected / exposed | 19 / 391 (4.86%) | 4 / 57 (7.02%) | 15 / 395 (3.80%) |
| occurrences (all) | 21 | 6 | 19 |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 12 / 391 (3.07%) | 7 / 57 (12.28%) | 7 / 395 (1.77%) |
| occurrences (all) | 13 | 8 | 8 |
| Muscular weakness | | | |
| subjects affected / exposed | 14 / 391 (3.58%) | 5 / 57 (8.77%) | 15 / 395 (3.80%) |
| occurrences (all) | 16 | 5 | 15 |
| Back pain | | | |
| subjects affected / exposed | 51 / 391 (13.04%) | 9 / 57 (15.79%) | 47 / 395 (11.90%) |
| occurrences (all) | 57 | 10 | 52 |
| Arthritis | | | |
| subjects affected / exposed | 6 / 391 (1.53%) | 3 / 57 (5.26%) | 3 / 395 (0.76%) |
| occurrences (all) | 6 | 3 | 6 |
| Arthralgia | | | |
| subjects affected / exposed | 63 / 391 (16.11%) | 9 / 57 (15.79%) | 44 / 395 (11.14%) |
| occurrences (all) | 76 | 11 | 50 |
| Infections and infestations | | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 24 / 391 (6.14%) | 4 / 57 (7.02%) | 11 / 395 (2.78%) |
| occurrences (all) | 30 | 4 | 15 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 23 / 391 (5.88%) | 6 / 57 (10.53%) | 23 / 395 (5.82%) |
| occurrences (all) | 33 | 7 | 25 |
| Pneumonia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 23 / 391 (5.88%) | 4 / 57 (7.02%) | 17 / 395 (4.30%) |
| occurrences (all) | 25 | 6 | 17 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 29 / 391 (7.42%) | 0 / 57 (0.00%) | 14 / 395 (3.54%) |
| occurrences (all) | 36 | 0 | 20 |
| Bronchitis | | | |
| subjects affected / exposed | 18 / 391 (4.60%) | 4 / 57 (7.02%) | 23 / 395 (5.82%) |
| occurrences (all) | 21 | 4 | 25 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 96 / 391 (24.55%) | 22 / 57 (38.60%) | 83 / 395 (21.01%) |
| occurrences (all) | 115 | 27 | 94 |
| Dehydration | | | |
| subjects affected / exposed | 26 / 391 (6.65%) | 12 / 57 (21.05%) | 12 / 395 (3.04%) |
| occurrences (all) | 31 | 12 | 13 |
| Hyperglycaemia | | | |
| subjects affected / exposed | 12 / 391 (3.07%) | 8 / 57 (14.04%) | 21 / 395 (5.32%) |
| occurrences (all) | 15 | 9 | 24 |
| Hypoalbuminaemia | | | |
| subjects affected / exposed | 8 / 391 (2.05%) | 8 / 57 (14.04%) | 8 / 395 (2.03%) |
| occurrences (all) | 12 | 10 | 10 |
| Hypocalcaemia | | | |
| subjects affected / exposed | 11 / 391 (2.81%) | 3 / 57 (5.26%) | 9 / 395 (2.28%) |
| occurrences (all) | 17 | 3 | 10 |
| Hypokalaemia | | | |
| subjects affected / exposed | 31 / 391 (7.93%) | 18 / 57 (31.58%) | 24 / 395 (6.08%) |
| occurrences (all) | 56 | 25 | 28 |
| Hypomagnesaemia | | | |
| subjects affected / exposed | 12 / 391 (3.07%) | 6 / 57 (10.53%) | 4 / 395 (1.01%) |
| occurrences (all) | 16 | 6 | 4 |
| Hyponatraemia | | | |
| subjects affected / exposed | 18 / 391 (4.60%) | 12 / 57 (21.05%) | 29 / 395 (7.34%) |
| occurrences (all) | 24 | 17 | 34 |

| **Non-serious adverse events** | Cohort A1 | | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 174 / 198 (87.88%) | | |
| Vascular disorders | | | |
| Hypotension | | | |
| subjects affected / exposed | 5 / 198 (2.53%) | | |
| occurrences (all) | 5 | | |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 25 / 198 (12.63%) | | |
| occurrences (all) | 29 | | |
| Pain | | | |
| subjects affected / exposed | 6 / 198 (3.03%) | | |
| occurrences (all) | 6 | | |
| Oedema peripheral | | | |
| subjects affected / exposed | 14 / 198 (7.07%) | | |
| occurrences (all) | 17 | | |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 8 / 198 (4.04%) | | |
| occurrences (all) | 8 | | |
| Malaise | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | |
| occurrences (all) | 1 | | |
| Localised oedema | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | |
| occurrences (all) | 1 | | |
| Fatigue | | | |
| subjects affected / exposed | 39 / 198 (19.70%) | | |
| occurrences (all) | 51 | | |
| Chills | | | |
| subjects affected / exposed | 2 / 198 (1.01%) | | |
| occurrences (all) | 2 | | |
| Asthenia | | | |
| subjects affected / exposed | 45 / 198 (22.73%) | | |
| occurrences (all) | 55 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Productive cough | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 13 / 198 (6.57%) | | |
| occurrences (all) | 14 | | |
| Pneumonitis | | | |
| subjects affected / exposed | 4 / 198 (2.02%) | | |
| occurrences (all) | 5 | | |
| Hypoxia | | | |
| subjects affected / exposed | 4 / 198 (2.02%) | | |
| occurrences (all) | 4 | | |
| Haemoptysis | | | |
| subjects affected / exposed | 10 / 198 (5.05%) | | |
| occurrences (all) | 11 | | |
| Dyspnoea | | | |
| subjects affected / exposed | 41 / 198 (20.71%) | | |
| occurrences (all) | 44 | | |
| Cough | | | |
| subjects affected / exposed | 22 / 198 (11.11%) | | |
| occurrences (all) | 25 | | |
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 5 / 198 (2.53%) | | |
| occurrences (all) | 7 | | |
| Nasal congestion | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | |
| occurrences (all) | 1 | | |
| Psychiatric disorders | | | |
| Insomnia | | | |
| subjects affected / exposed | 14 / 198 (7.07%) | | |
| occurrences (all) | 14 | | |
| Depression | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | |
| occurrences (all) | 1 | | |
| Anxiety | | | |
| subjects affected / exposed | 8 / 198 (4.04%) | | |
| occurrences (all) | 9 | | |
| Investigations | | | |

| | | | |
|---|---|---|---|
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 12 / 198 (6.06%) | | |
| occurrences (all) | 22 | | |
| Amylase increased | | | |
| subjects affected / exposed | 19 / 198 (9.60%) | | |
| occurrences (all) | 27 | | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 11 / 198 (5.56%) | | |
| occurrences (all) | 20 | | |
| Blood alkaline phosphatase increased | | | |
| subjects affected / exposed | 8 / 198 (4.04%) | | |
| occurrences (all) | 11 | | |
| Blood creatinine increased | | | |
| subjects affected / exposed | 11 / 198 (5.56%) | | |
| occurrences (all) | 11 | | |
| Lipase increased | | | |
| subjects affected / exposed | 18 / 198 (9.09%) | | |
| occurrences (all) | 21 | | |
| Lymphocyte count decreased | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences (all) | 0 | | |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | |
| occurrences (all) | 1 | | |
| Weight decreased | | | |
| subjects affected / exposed | 16 / 198 (8.08%) | | |
| occurrences (all) | 17 | | |
| Weight increased | | | |
| subjects affected / exposed | 2 / 198 (1.01%) | | |
| occurrences (all) | 2 | | |
| Injury, poisoning and procedural complications | | | |
| Fall | | | |
| subjects affected / exposed | 2 / 198 (1.01%) | | |
| occurrences (all) | 2 | | |
| Infusion related reaction | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed<br>occurrences (all) | 2 / 198 (1.01%)<br>2 | | |
| Cardiac disorders<br>Atrial fibrillation<br>subjects affected / exposed<br>occurrences (all) | <br><br>6 / 198 (3.03%)<br>6 | | |
| Nervous system disorders<br>Peripheral sensory neuropathy<br>subjects affected / exposed<br>occurrences (all)<br><br>Headache<br>subjects affected / exposed<br>occurrences (all)<br><br>Dizziness<br>subjects affected / exposed<br>occurrences (all) | <br><br>0 / 198 (0.00%)<br>0<br><br><br>26 / 198 (13.13%)<br>32<br><br><br>15 / 198 (7.58%)<br>17 | | |
| Blood and lymphatic system disorders<br>Anaemia<br>subjects affected / exposed<br>occurrences (all) | <br><br>35 / 198 (17.68%)<br>44 | | |
| Eye disorders<br>Vision blurred<br>subjects affected / exposed<br>occurrences (all)<br><br>Dry eye<br>subjects affected / exposed<br>occurrences (all) | <br><br>6 / 198 (3.03%)<br>6<br><br><br>1 / 198 (0.51%)<br>1 | | |
| Gastrointestinal disorders<br>Gastrooesophageal reflux disease<br>subjects affected / exposed<br>occurrences (all)<br><br>Dysphagia<br>subjects affected / exposed<br>occurrences (all)<br><br>Dry mouth<br>subjects affected / exposed<br>occurrences (all) | <br><br>1 / 198 (0.51%)<br>1<br><br><br>4 / 198 (2.02%)<br>4<br><br><br>4 / 198 (2.02%)<br>4 | | |

| | | | |
|---|---|---|---|
| Diarrhoea | | | |
| subjects affected / exposed | 48 / 198 (24.24%) | | |
| occurrences (all) | 58 | | |
| Constipation | | | |
| subjects affected / exposed | 26 / 198 (13.13%) | | |
| occurrences (all) | 28 | | |
| Colitis | | | |
| subjects affected / exposed | 7 / 198 (3.54%) | | |
| occurrences (all) | 9 | | |
| Abdominal pain | | | |
| subjects affected / exposed | 5 / 198 (2.53%) | | |
| occurrences (all) | 7 | | |
| Nausea | | | |
| subjects affected / exposed | 40 / 198 (20.20%) | | |
| occurrences (all) | 51 | | |
| Vomiting | | | |
| subjects affected / exposed | 18 / 198 (9.09%) | | |
| occurrences (all) | 25 | | |
| Oral pain | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences (all) | 0 | | |
| Skin and subcutaneous tissue disorders | | | |
| Rash | | | |
| subjects affected / exposed | 31 / 198 (15.66%) | | |
| occurrences (all) | 45 | | |
| Pruritus | | | |
| subjects affected / exposed | 32 / 198 (16.16%) | | |
| occurrences (all) | 39 | | |
| Erythema | | | |
| subjects affected / exposed | 6 / 198 (3.03%) | | |
| occurrences (all) | 7 | | |
| Dry skin | | | |
| subjects affected / exposed | 9 / 198 (4.55%) | | |
| occurrences (all) | 9 | | |
| Rash maculo-papular | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed<br>occurrences (all) | 6 / 198 (3.03%)<br>9 | | |
| Endocrine disorders<br>Hypothyroidism<br>subjects affected / exposed<br>occurrences (all)<br><br>Hyperthyroidism<br>subjects affected / exposed<br>occurrences (all)<br><br>Adrenal insufficiency<br>subjects affected / exposed<br>occurrences (all) | <br><br>14 / 198 (7.07%)<br>17<br><br><br>17 / 198 (8.59%)<br>17<br><br><br>4 / 198 (2.02%)<br>4 | | |
| Musculoskeletal and connective tissue disorders<br>Pain in extremity<br>subjects affected / exposed<br>occurrences (all)<br><br>Myalgia<br>subjects affected / exposed<br>occurrences (all)<br><br>Musculoskeletal chest pain<br>subjects affected / exposed<br>occurrences (all)<br><br>Muscular weakness<br>subjects affected / exposed<br>occurrences (all)<br><br>Back pain<br>subjects affected / exposed<br>occurrences (all)<br><br>Arthritis<br>subjects affected / exposed<br>occurrences (all)<br><br>Arthralgia<br>subjects affected / exposed<br>occurrences (all) | <br><br>7 / 198 (3.54%)<br>9<br><br><br>3 / 198 (1.52%)<br>3<br><br><br>1 / 198 (0.51%)<br>3<br><br><br>5 / 198 (2.53%)<br>5<br><br><br>15 / 198 (7.58%)<br>15<br><br><br>7 / 198 (3.54%)<br>7<br><br><br>25 / 198 (12.63%)<br>27 | | |
| Infections and infestations | | | |

| | | | | |
|---|---|---|---|---|
| Urinary tract infection<br>subjects affected / exposed<br>occurrences (all) | 7 / 198 (3.54%)<br>8 | | | |
| Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all) | 6 / 198 (3.03%)<br>8 | | | |
| Pneumonia<br>subjects affected / exposed<br>occurrences (all) | 15 / 198 (7.58%)<br>15 | | | |
| Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all) | 10 / 198 (5.05%)<br>11 | | | |
| Bronchitis<br>subjects affected / exposed<br>occurrences (all) | 8 / 198 (4.04%)<br>9 | | | |
| Metabolism and nutrition disorders<br>Decreased appetite<br>subjects affected / exposed<br>occurrences (all) | 38 / 198 (19.19%)<br>46 | | | |
| Dehydration<br>subjects affected / exposed<br>occurrences (all) | 6 / 198 (3.03%)<br>8 | | | |
| Hyperglycaemia<br>subjects affected / exposed<br>occurrences (all) | 11 / 198 (5.56%)<br>11 | | | |
| Hypoalbuminaemia<br>subjects affected / exposed<br>occurrences (all) | 4 / 198 (2.02%)<br>6 | | | |
| Hypocalcaemia<br>subjects affected / exposed<br>occurrences (all) | 7 / 198 (3.54%)<br>7 | | | |
| Hypokalaemia<br>subjects affected / exposed<br>occurrences (all) | 12 / 198 (6.06%)<br>15 | | | |
| Hypomagnesaemia | | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 4 / 198 (2.02%) | | |
| occurrences (all) | 5 | | |
| Hyponatraemia | | | |
| subjects affected / exposed | 13 / 198 (6.57%) | | |
| occurrences (all) | 18 | | |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 15 September 2016 | Management Algorithms updated |
| 09 November 2016 | Study design and exclusion criteria updated |
| 27 July 2017 | Study design and new study personnel updated |
| 25 October 2017 | Study design updated |
| 04 June 2018 | Endpoints for Cohort C updated |
| 02 July 2019 | Updated FACT-L collection during survival follow-up |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported