# Clinical trial results:
# A Phase 1 Study of the EZH2 Inhibitor Tazemetostat in Pediatric Subjects with Relapsed or Refractory INI1-Negative Tumors or Synovial Sarcoma

## Summary

| | |
|---|---|
| EudraCT number | 2015-002468-18 |
| Trial protocol | GB DK DE NL IT |
| Global end of trial date | 19 June 2021 |

### Results information

| | |
|---|---|
| Result version number | v2 (current) |
| This version publication date | 13 July 2024 |
| First version publication date | 11 January 2022 |
| Version creation reason | • Correction of full data set<br>Correction of full data set |

## Trial information

### Trial identification

| | |
|---|---|
| Sponsor protocol code | EZH-102 |

### Additional study identifiers

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02601937 |
| WHO universal trial number (UTN) | - |

Notes:

### Sponsors

| | |
|---|---|
| Sponsor organisation name | Epizyme, Inc. |
| Sponsor organisation address | 400 Technology Square, 4th Floor, Cambridge, United States, 02139 |
| Public contact | Shefali Agarwal, MBBS, MPH, MIS, Epizyme, Inc., 001 855500-1011, clinicaltrials@epizyme.com |
| Scientific contact | Shefali Agarwal, MBBS, MPH, MIS, Epizyme, Inc., 001 855500-1011, clinicaltrials@epizyme.com |

Notes:

### Paediatric regulatory details

| | |
|---|---|
| Is trial part of an agreed paediatric investigation plan (PIP) | Yes |
| EMA paediatric investigation plan number(s) | EMEA-003055-PIP01-21 |
| 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 | 22 October 2021 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 19 June 2021 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

Dose Escalation: To determine the maximum tolerated dose (MTD) or the recommended phase 2 dose (RP2D) of tazemetostat when administered as an oral suspension twice daily (BID) in pediatric subjects with relapsed/refractory rhabdoid tumors, integrase interactor 1 (INI1)-negative tumors or synovial sarcoma.

Dose Expansion: To evaluate the antitumor activity of tazemetostat as assessed by overall response rate (ORR) in pediatric subjects with relapsed/refractory atypical teratoid rhabdoid tumor (ATRT) (Cohort 1), non-ATRT rhabdoid tumors (Cohort 2), INI1-negative tumors (Cohort 3), and tumor types eligible for Cohorts 1 through 3 or synovial sarcoma with SS18-SSX rearrangement (Cohort 4) using disease-appropriate standardized response criteria.

Protection of trial subjects:

The procedures set out in the study protocol pertaining to the conduct, evaluation, and documentation of this study were designed to ensure that the Sponsor and Investigators are by Good Clinical Practice (GCP) as described in the International Conference on Harmonisation (ICH) Tripartite Guideline E6. Compliance with these regulations also constituted compliance with the ethical principles described in the current revision of the Declaration of Helsinki. The study was also carried out in keeping with local legal and regulatory requirements. Subject confidentiality was strictly held in trust by the Sponsor and/or their designee(s), participating Investigators, and site staff.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 07 January 2016 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Safety, Efficacy |
| Long term follow-up duration | 2 Years |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Netherlands: 3 |
| Country: Number of subjects enrolled | United Kingdom: 7 |
| Country: Number of subjects enrolled | Denmark: 12 |
| Country: Number of subjects enrolled | France: 14 |
| Country: Number of subjects enrolled | Germany: 1 |
| Country: Number of subjects enrolled | Italy: 7 |
| Country: Number of subjects enrolled | Australia: 7 |
| Country: Number of subjects enrolled | United States: 55 |
| Country: Number of subjects enrolled | Canada: 3 |

| | |
|---|---|
| Worldwide total number of subjects | 109 |
| EEA total number of subjects | 37 |

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) | 17 |
| Children (2-11 years) | 62 |
| Adolescents (12-17 years) | 27 |
| Adults (18-64 years) | 3 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

07 January 2016 – 19 June 2021; Medical clinics, hospitals, and academic research centers.

### Pre-assignment

Screening details:

A signed, written informed consent (and assent, if applicable) must be obtained prior to any study-specific assessments or procedures being performed. All Screening assessments must be performed within 14 days prior to enrollment (Screening Period extends from Day -14 to Day -1).

### 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** | Dose Escalation Level 1 |

Arm description:

Subjects with relapsed/refractory rhabdoid tumors, INI1-negative tumors, or synovial sarcoma with SS18-SSX rearrangement received oral tazemetostat 240 milligrams per square meter (mg/m^2) BID in continuous 28-day cycles.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Tazemostat |
| Investigational medicinal product code | EPZ-6438 |
| Other name | E7438 |
| Pharmaceutical forms | Suspension for oral suspension |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received tazemetostat oral suspension. The amount of tazemetostat oral suspension per dose is calculated based on the subject’s body surface area (BSA) and the assigned dose level. Subjects received oral suspension at the assigned dose twice daily.

| | |
|---|---|
| **Arm title** | Dose Escalation Level 2 |

Arm description:

Subjects with relapsed/refractory rhabdoid tumors, INI1-negative tumors, or synovial sarcoma with SS18-SSX rearrangement received oral tazemetostat 300 mg/m^2 BID in continuous 28-day cycles.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Tazemostat |
| Investigational medicinal product code | EPZ-6438 |
| Other name | E7438 |
| Pharmaceutical forms | Suspension for oral suspension |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received tazemetostat oral suspension. The amount of tazemetostat oral suspension per dose is calculated based on the subject’s body surface area (BSA) and the assigned dose level. Subjects received oral suspension at the assigned dose twice daily.

| | |
|---|---|
| **Arm title** | Dose Escalation Level 3 |

Arm description:

Subjects with relapsed/refractory rhabdoid tumors, INI1-negative tumors, or synovial sarcoma with SS18-SSX rearrangement received oral tazemetostat 400 mg/m^2 BID in continuous 28-day cycles.

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

| | |
|---|---|
| Investigational medicinal product name | Tazemostat |
| Investigational medicinal product code | EPZ-6438 |
| Other name | E7438 |
| Pharmaceutical forms | Suspension for oral suspension |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received tazemetostat oral suspension. The amount of tazemetostat oral suspension per dose is calculated based on the subject's body surface area (BSA) and the assigned dose level. Subjects received oral suspension at the assigned dose twice daily.

| | |
|---|---|
| **Arm title** | Dose Escalation Level 4 |

Arm description:

Subjects with relapsed/refractory rhabdoid tumors, INI1-negative tumors, or synovial sarcoma with SS18-SSX rearrangement received oral tazemetostat 520 mg/m^2 BID in continuous 28-day cycles.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Tazemostat |
| Investigational medicinal product code | EPZ-6438 |
| Other name | E7438 |
| Pharmaceutical forms | Suspension for oral suspension |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received tazemetostat oral suspension. The amount of tazemetostat oral suspension per dose is calculated based on the subject's body surface area (BSA) and the assigned dose level. Subjects received oral suspension at the assigned dose twice daily.

| | |
|---|---|
| **Arm title** | Dose Escalation Level 5 |

Arm description:

Subjects with relapsed/refractory rhabdoid tumors, INI1-negative tumors, or synovial sarcoma with SS18-SSX rearrangement received oral tazemetostat 700 mg/m^2 BID in continuous 28-day cycles.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Tazemostat |
| Investigational medicinal product code | EPZ-6438 |
| Other name | E7438 |
| Pharmaceutical forms | Suspension for oral suspension |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received tazemetostat oral suspension. The amount of tazemetostat oral suspension per dose is calculated based on the subject's body surface area (BSA) and the assigned dose level. Subjects received oral suspension at the assigned dose twice daily.

| | |
|---|---|
| **Arm title** | Dose Escalation Level 6 |

Arm description:

Subjects with relapsed/refractory rhabdoid tumors, INI1-negative tumors, or synovial sarcoma with SS18-SSX rearrangement received oral tazemetostat 900 mg/m^2 BID in continuous 28-day cycles.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Tazemostat |
| Investigational medicinal product code | EPZ-6438 |
| Other name | E7438 |
| Pharmaceutical forms | Suspension for oral suspension |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received tazemetostat oral suspension. The amount of tazemetostat oral suspension per dose is calculated based on the subject's body surface area (BSA) and the assigned dose level. Subjects received oral suspension at the assigned dose twice daily.

| | |
|---|---|
| **Arm title** | Dose Escalation Level 7 |

Arm description:

Subjects with relapsed/refractory rhabdoid tumors, INI1-negative tumors, or synovial sarcoma with

SS18-SSX rearrangement received oral tazemetostat 1200 mg/m^2 BID in continuous 28-day cycles.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Tazemostat |
| Investigational medicinal product code | EPZ-6438 |
| Other name | E7438 |
| Pharmaceutical forms | Suspension for oral suspension |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received tazemetostat oral suspension. The amount of tazemetostat oral suspension per dose is calculated based on the subject's body surface area (BSA) and the assigned dose level. Subjects received oral suspension at the assigned dose twice daily.

| | |
|---|---|
| **Arm title** | Dose Expansion Cohort 1 |

Arm description:

Subjects with atypical teratoid rhabdoid tumor (ATRT) who participated in the dose expansion portion of the study received 1200 mg/m^2 open-label, tazemetostat BID orally in continuous 28-day cycles.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Tazemostat |
| Investigational medicinal product code | EPZ-6438 |
| Other name | E7438 |
| Pharmaceutical forms | Suspension for oral suspension |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received tazemetostat oral suspension. The amount of tazemetostat oral suspension per dose is calculated based on the subject's body surface area (BSA) and the assigned dose level. Subjects received oral suspension at the assigned dose twice daily.

| | |
|---|---|
| **Arm title** | Dose Expansion Cohort 2 |

Arm description:

Subjects with malignant rhabdoid tumor (MRT)/ rhabdoid tumor of kidney (RTK)/select tumors with rhabdoid features who participated in the dose expansion portion of the study. Subjects whose disease was without central nervous system (CNS) involvement received 520 mg/m^2 open-label, tazemetostat BID orally in continuous 28-day cycles. Subjects whose disease had CNS involvement received 1200 mg/m^2 open-label, tazemetostat BID orally in continuous 28-day cycles.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Tazemostat |
| Investigational medicinal product code | EPZ-6438 |
| Other name | E7438 |
| Pharmaceutical forms | Suspension for oral suspension |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received tazemetostat oral suspension. The amount of tazemetostat oral suspension per dose is calculated based on the subject's body surface area (BSA) and the assigned dose level. Subjects received oral suspension at the assigned dose twice daily.

| | |
|---|---|
| **Arm title** | Dose Expansion Cohort 3 |

Arm description:

Subjects with INI-negative tumors who participated in the dose expansion portion of the study. Subjects whose disease was without central nervous system (CNS) involvement received 520 mg/m^2 open-label, tazemetostat BID orally in continuous 28-day cycles. Subjects whose disease had CNS involvement received 1200 mg/m^2 open-label, tazemetostat BID orally in continuous 28-day cycles.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Tazemostat |
| Investigational medicinal product code | EPZ-6438 |
| Other name | E7438 |
| Pharmaceutical forms | Suspension for oral suspension |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects received tazemetostat oral suspension. The amount of tazemetostat oral suspension per dose is calculated based on the subject's body surface area (BSA) and the assigned dose level. Subjects received oral suspension at the assigned dose twice daily.

| **Arm title** | Dose Expansion Cohort 4 |
|---|---|

Arm description:

Subjects with one of the tumor types defined in Cohorts 1 through 3 or synovial sarcoma with SS18-SSX rearrangement received 800 mg/m^2 tazemetostat three times daily (TID) orally in continuous 28-day cycles.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Tazemostat |
| Investigational medicinal product code | EPZ-6438 |
| Other name | E7438 |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects in Dose Expansion Cohort 4 received tazemetostat tablet formulation, 800 mg/m2 three times daily (2400 mg/m2/day equivalent to 1200 mg/m2 BID).

| **Number of subjects in period 1** | Dose Escalation Level 1 | Dose Escalation Level 2 | Dose Escalation Level 3 |
|---|---|---|---|
| Started | 8 | 6 | 6 |
| Completed | 0 | 0 | 0 |
| Not completed | 8 | 6 | 6 |
| Physician decision | - | - | - |
| death | - | - | - |
| unknown | - | - | - |
| Adverse event, non-fatal | - | - | - |
| Subject refused further treatment of study drug | 1 | - | - |
| Unacceptable toxicity | - | - | 1 |
| Disease Progression | 7 | 6 | 5 |

| **Number of subjects in period 1** | Dose Escalation Level 4 | Dose Escalation Level 5 | Dose Escalation Level 6 |
|---|---|---|---|
| Started | 7 | 6 | 6 |
| Completed | 1 | 0 | 1 |
| Not completed | 6 | 6 | 5 |
| Physician decision | - | - | - |
| death | - | - | - |
| unknown | - | - | - |
| Adverse event, non-fatal | - | - | 1 |
| Subject refused further treatment of study drug | - | - | - |
| Unacceptable toxicity | - | - | - |

| | | | |
|---|---|---|---|
| Disease Progression | 6 | 6 | 4 |

| **Number of subjects in period 1** | Dose Escalation Level 7 | Dose Expansion Cohort 1 | Dose Expansion Cohort 2 |
|---|---|---|---|
| Started | 7 | 19 | 20 |
| Completed | 0 | 1 | 0 |
| Not completed | 7 | 18 | 20 |
| Physician decision | - | - | - |
| death | - | - | 1 |
| unknown | - | - | 2 |
| Adverse event, non-fatal | - | - | - |
| Subject refused further treatment of study drug | 1 | 2 | - |
| Unacceptable toxicity | - | - | - |
| Disease Progression | 6 | 16 | 17 |

| **Number of subjects in period 1** | Dose Expansion Cohort 3 | Dose Expansion Cohort 4 |
|---|---|---|
| Started | 18 | 6 |
| Completed | 0 | 1 |
| Not completed | 18 | 5 |
| Physician decision | 1 | 1 |
| death | - | - |
| unknown | 2 | - |
| Adverse event, non-fatal | 1 | - |
| Subject refused further treatment of study drug | - | - |
| Unacceptable toxicity | - | - |
| Disease Progression | 14 | 4 |

## Baseline characteristics

### Reporting groups

| Reporting group title | Dose Escalation Level 1 |
|---|---|

Reporting group description:

Subjects with relapsed/refractory rhabdoid tumors, INI1-negative tumors, or synovial sarcoma with SS18-SSX rearrangement received oral tazemetostat 240 milligrams per square meter (mg/m^2) BID in continuous 28-day cycles.

| Reporting group title | Dose Escalation Level 2 |
|---|---|

Reporting group description:

Subjects with relapsed/refractory rhabdoid tumors, INI1-negative tumors, or synovial sarcoma with SS18-SSX rearrangement received oral tazemetostat 300 mg/m^2 BID in continuous 28-day cycles.

| Reporting group title | Dose Escalation Level 3 |
|---|---|

Reporting group description:

Subjects with relapsed/refractory rhabdoid tumors, INI1-negative tumors, or synovial sarcoma with SS18-SSX rearrangement received oral tazemetostat 400 mg/m^2 BID in continuous 28-day cycles.

| Reporting group title | Dose Escalation Level 4 |
|---|---|

Reporting group description:

Subjects with relapsed/refractory rhabdoid tumors, INI1-negative tumors, or synovial sarcoma with SS18-SSX rearrangement received oral tazemetostat 520 mg/m^2 BID in continuous 28-day cycles.

| Reporting group title | Dose Escalation Level 5 |
|---|---|

Reporting group description:

Subjects with relapsed/refractory rhabdoid tumors, INI1-negative tumors, or synovial sarcoma with SS18-SSX rearrangement received oral tazemetostat 700 mg/m^2 BID in continuous 28-day cycles.

| Reporting group title | Dose Escalation Level 6 |
|---|---|

Reporting group description:

Subjects with relapsed/refractory rhabdoid tumors, INI1-negative tumors, or synovial sarcoma with SS18-SSX rearrangement received oral tazemetostat 900 mg/m^2 BID in continuous 28-day cycles.

| Reporting group title | Dose Escalation Level 7 |
|---|---|

Reporting group description:

Subjects with relapsed/refractory rhabdoid tumors, INI1-negative tumors, or synovial sarcoma with SS18-SSX rearrangement received oral tazemetostat 1200 mg/m^2 BID in continuous 28-day cycles.

| Reporting group title | Dose Expansion Cohort 1 |
|---|---|

Reporting group description:

Subjects with atypical teratoid rhabdoid tumor (ATRT) who participated in the dose expansion portion of the study received 1200 mg/m^2 open-label, tazemetostat BID orally in continuous 28-day cycles.

| Reporting group title | Dose Expansion Cohort 2 |
|---|---|

Reporting group description:

Subjects with malignant rhabdoid tumor (MRT)/ rhabdoid tumor of kidney (RTK)/select tumors with rhabdoid features who participated in the dose expansion portion of the study. Subjects whose disease was without central nervous system (CNS) involvement received 520 mg/m^2 open-label, tazemetostat BID orally in continuous 28-day cycles. Subjects whose disease had CNS involvement received 1200 mg/m^2 open-label, tazemetostat BID orally in continuous 28-day cycles.

| Reporting group title | Dose Expansion Cohort 3 |
|---|---|

Reporting group description:

Subjects with INI-negative tumors who participated in the dose expansion portion of the study. Subjects whose disease was without central nervous system (CNS) involvement received 520 mg/m^2 open-label, tazemetostat BID orally in continuous 28-day cycles. Subjects whose disease had CNS involvement received 1200 mg/m^2 open-label, tazemetostat BID orally in continuous 28-day cycles.

| Reporting group title | Dose Expansion Cohort 4 |
|---|---|

Reporting group description:

Subjects with one of the tumor types defined in Cohorts 1 through 3 or synovial sarcoma with SS18-SSX rearrangement received 800 mg/m^2 tazemetostat three times daily (TID) orally in continuous 28-day cycles.

| Reporting group values | Dose Escalation Level 1 | Dose Escalation Level 2 | Dose Escalation Level 3 |
|---|---|---|---|
| Number of subjects | 8 | 6 | 6 |
| Age categorical<br>Units: Subjects | | | |
| Infants and toddlers (28 days-23 months) | 4 | 1 | 1 |
| Children (2-11 years) | 4 | 0 | 4 |
| Adolescents (12-17 years) | 0 | 5 | 1 |
| Adults (18-64 years) | 0 | 0 | 0 |
| Gender categorical<br>Units: Subjects | | | |
| Female | 4 | 4 | 5 |
| Male | 4 | 2 | 1 |
| Race<br>Units: Subjects | | | |
| Asian | 0 | 0 | 1 |
| Black or African American | 1 | 0 | 0 |
| White | 7 | 6 | 4 |
| Unknown or Not Reported | 0 | 0 | 1 |
| Ethnicity<br>Units: Subjects | | | |
| Hispanic or Latino | 0 | 0 | 3 |
| Not Hispanic or Latino | 8 | 4 | 2 |
| Unknown or Not Reported | 0 | 2 | 1 |

| Reporting group values | Dose Escalation Level 4 | Dose Escalation Level 5 | Dose Escalation Level 6 |
|---|---|---|---|
| Number of subjects | 7 | 6 | 6 |
| Age categorical<br>Units: Subjects | | | |
| Infants and toddlers (28 days-23 months) | 1 | 0 | 1 |
| Children (2-11 years) | 6 | 4 | 5 |
| Adolescents (12-17 years) | 0 | 2 | 0 |
| Adults (18-64 years) | 0 | 0 | 0 |
| Gender categorical<br>Units: Subjects | | | |
| Female | 5 | 2 | 4 |
| Male | 2 | 4 | 2 |
| Race<br>Units: Subjects | | | |
| Asian | 1 | 0 | 1 |
| Black or African American | 1 | 1 | 1 |
| White | 5 | 4 | 4 |
| Unknown or Not Reported | 0 | 1 | 0 |
| Ethnicity<br>Units: Subjects | | | |
| Hispanic or Latino | 0 | 1 | 0 |
| Not Hispanic or Latino | 7 | 4 | 5 |
| Unknown or Not Reported | 0 | 1 | 1 |

| Reporting group values | Dose Escalation | Dose Expansion | Dose Expansion |
|---|---|---|---|

| | Level 7 | Cohort 1 | Cohort 2 |
|---|---|---|---|
| Number of subjects | 7 | 19 | 20 |
| Age categorical<br>Units: Subjects | | | |
| Infants and toddlers (28 days-23 months) | 2 | 2 | 5 |
| Children (2-11 years) | 4 | 15 | 13 |
| Adolescents (12-17 years) | 1 | 2 | 2 |
| Adults (18-64 years) | 0 | 0 | 0 |
| Gender categorical<br>Units: Subjects | | | |
| Female | 2 | 12 | 7 |
| Male | 5 | 7 | 13 |
| Race<br>Units: Subjects | | | |
| Asian | 0 | 0 | 1 |
| Black or African American | 1 | 2 | 0 |
| White | 5 | 14 | 12 |
| Unknown or Not Reported | 1 | 3 | 7 |
| Ethnicity<br>Units: Subjects | | | |
| Hispanic or Latino | 1 | 5 | 2 |
| Not Hispanic or Latino | 5 | 13 | 14 |
| Unknown or Not Reported | 1 | 1 | 4 |

| **Reporting group values** | Dose Expansion Cohort 3 | Dose Expansion Cohort 4 | Total |
|---|---|---|---|
| Number of subjects | 18 | 6 | 109 |
| Age categorical<br>Units: Subjects | | | |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 17 |
| Children (2-11 years) | 5 | 2 | 62 |
| Adolescents (12-17 years) | 12 | 2 | 27 |
| Adults (18-64 years) | 1 | 2 | 3 |
| Gender categorical<br>Units: Subjects | | | |
| Female | 11 | 3 | 59 |
| Male | 7 | 3 | 50 |
| Race<br>Units: Subjects | | | |
| Asian | 0 | 0 | 4 |
| Black or African American | 1 | 0 | 8 |
| White | 14 | 4 | 79 |
| Unknown or Not Reported | 3 | 2 | 18 |
| Ethnicity<br>Units: Subjects | | | |
| Hispanic or Latino | 4 | 1 | 17 |
| Not Hispanic or Latino | 12 | 5 | 79 |
| Unknown or Not Reported | 2 | 0 | 13 |

## End points

### End points reporting groups

| Reporting group title | Dose Escalation Level 1 |
|---|---|
| Reporting group description: | |
| Subjects with relapsed/refractory rhabdoid tumors, INI1-negative tumors, or synovial sarcoma with SS18-SSX rearrangement received oral tazemetostat 240 milligrams per square meter (mg/m^2) BID in continuous 28-day cycles. | |
| Reporting group title | Dose Escalation Level 2 |
| Reporting group description: | |
| Subjects with relapsed/refractory rhabdoid tumors, INI1-negative tumors, or synovial sarcoma with SS18-SSX rearrangement received oral tazemetostat 300 mg/m^2 BID in continuous 28-day cycles. | |
| Reporting group title | Dose Escalation Level 3 |
| Reporting group description: | |
| Subjects with relapsed/refractory rhabdoid tumors, INI1-negative tumors, or synovial sarcoma with SS18-SSX rearrangement received oral tazemetostat 400 mg/m^2 BID in continuous 28-day cycles. | |
| Reporting group title | Dose Escalation Level 4 |
| Reporting group description: | |
| Subjects with relapsed/refractory rhabdoid tumors, INI1-negative tumors, or synovial sarcoma with SS18-SSX rearrangement received oral tazemetostat 520 mg/m^2 BID in continuous 28-day cycles. | |
| Reporting group title | Dose Escalation Level 5 |
| Reporting group description: | |
| Subjects with relapsed/refractory rhabdoid tumors, INI1-negative tumors, or synovial sarcoma with SS18-SSX rearrangement received oral tazemetostat 700 mg/m^2 BID in continuous 28-day cycles. | |
| Reporting group title | Dose Escalation Level 6 |
| Reporting group description: | |
| Subjects with relapsed/refractory rhabdoid tumors, INI1-negative tumors, or synovial sarcoma with SS18-SSX rearrangement received oral tazemetostat 900 mg/m^2 BID in continuous 28-day cycles. | |
| Reporting group title | Dose Escalation Level 7 |
| Reporting group description: | |
| Subjects with relapsed/refractory rhabdoid tumors, INI1-negative tumors, or synovial sarcoma with SS18-SSX rearrangement received oral tazemetostat 1200 mg/m^2 BID in continuous 28-day cycles. | |
| Reporting group title | Dose Expansion Cohort 1 |
| Reporting group description: | |
| Subjects with atypical teratoid rhabdoid tumor (ATRT) who participated in the dose expansion portion of the study received 1200 mg/m^2 open-label, tazemetostat BID orally in continuous 28-day cycles. | |
| Reporting group title | Dose Expansion Cohort 2 |
| Reporting group description: | |
| Subjects with malignant rhabdoid tumor (MRT)/ rhabdoid tumor of kidney (RTK)/select tumors with rhabdoid features who participated in the dose expansion portion of the study. Subjects whose disease was without central nervous system (CNS) involvement received 520 mg/m^2 open-label, tazemetostat BID orally in continuous 28-day cycles. Subjects whose disease had CNS involvement received 1200 mg/m^2 open-label, tazemetostat BID orally in continuous 28-day cycles. | |
| Reporting group title | Dose Expansion Cohort 3 |
| Reporting group description: | |
| Subjects with INI-negative tumors who participated in the dose expansion portion of the study. Subjects whose disease was without central nervous system (CNS) involvement received 520 mg/m^2 open-label, tazemetostat BID orally in continuous 28-day cycles. Subjects whose disease had CNS involvement received 1200 mg/m^2 open-label, tazemetostat BID orally in continuous 28-day cycles. | |
| Reporting group title | Dose Expansion Cohort 4 |
| Reporting group description: | |
| Subjects with one of the tumor types defined in Cohorts 1 through 3 or synovial sarcoma with SS18-SSX rearrangement received 800 mg/m^2 tazemetostat three times daily (TID) orally in continuous 28-day cycles. | |

| | |
|---|---|
| Subject analysis set title | Overall Dose Escalation |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Subjects with relapsed/refractory rhabdoid tumors, INI1-negative tumors, or synovial sarcoma with SS18-SSX rearrangement received oral tazemetostat at dose Level 1: 240 mg/m^2 BID, dose level 2: 300 mg/m^2 BID, dose level 3: 400 mg/m^2 BID, dose level 4: 520 mg/m^2 BID, dose level 5: 700 mg/m^2 BID, dose level 6: 900 mg/m^2 BID and dose level 7: 1200 mg/m^2 BID in continuous 28-day cycles.

## Primary: Number of Dose-limiting Toxicities (Dose Escalation Only)

| | |
|---|---|
| End point title | Number of Dose-limiting Toxicities (Dose Escalation Only)[1][2] |

End point description:

The RP2D in pediatric subjects treated with tazemetostat as determined by the incidence and severity of treatment-emergent adverse events qualifying as protocol-defined dose-limiting toxicities that occurred during the first month of treatment. Dose-Limiting Toxicity (DLT) population included all subjects in the safety population set who experienced a DLT during Cycle 1 or were not removed from Cycle 1 for reasons other than toxicity and did not have an interruption in study treatment for more than 14 days during Cycle 1. Only those subjects with data collected at Cycle 1 are reported.

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

End point timeframe:

Cycle 1, from the start of study treatment (Day 1) until the end of the first Cycle (Day 28) of treatment

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: Summary statistics were provided for this study. This was a signal findings study that was not powered to make statistical comparisons.

[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: There are 8 different phases in the trial (7 dose escalation phases and the dose expansion phase with 4 cohorts) within the same period (overall study). All 8 phases are encompassed within the baseline period but the dose escalation and dose expansion phases have different end points.

| **End point values** | Dose Escalation Level 1 | Dose Escalation Level 2 | Dose Escalation Level 3 | Dose Escalation Level 4 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 5 | 6 | 6 | 6 |
| Units: number | 0 | 1 | 0 | 0 |

| **End point values** | Dose Escalation Level 5 | Dose Escalation Level 6 | Dose Escalation Level 7 | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 6 | 6 | 6 | |
| Units: number | 0 | 1 | 0 | |

### Statistical analyses

No statistical analyses for this end point

## Primary: Overall Response Rate (ORR) (dose expansion only)

| End point title | Overall Response Rate (ORR) (dose expansion only)[3][4] |
|---|---|

End point description:

ORR is defined as the percentage of subjects who achieved a confirmed CR and/or PR defined by RECIST or RANO criteria from the start of tazemetostat treatment until disease progression or the start of subsequent anticancer therapy, whichever occurs first. CR is defined as disappearance of all target and non-target lesions (with all lymph nodes must be non-pathological in size or under 10 millimeters [mm] in short axis) and PR is defined as at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters. ORR= CR+PR. The ITT population included all subjects who received at least one dose of tazemetostat.

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

End point timeframe:

RECIST assessments performed at screening (within 14 days before start of study intervention) and every 8 weeks post start of dosing, approximately up to 302 weeks

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: Summary statistics were provided for this study. This was a signal findings study that was not powered to make statistical comparisons.
[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: There are 8 different phases in the trial (7 dose escalation phases and the dose expansion phase with 4 cohorts) within the same period (overall study). All 8 phases are encompassed within the baseline period but the dose escalation and dose expansion phases have different end points.

| **End point values** | Dose Expansion Cohort 1 | Dose Expansion Cohort 2 | Dose Expansion Cohort 3 | Dose Expansion Cohort 4 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 19 | 20 | 18 | 6 |
| Units: Percentage of participants | | | | |
| number (not applicable) | 26.3 | 0 | 16.7 | 16.7 |

## Statistical analyses

No statistical analyses for this end point

## Primary: Recommended phase 2 dose (RP2D) (dose escalation only)

| End point title | Recommended phase 2 dose (RP2D) (dose escalation only)[5] |
|---|---|

End point description:

The incidence and severity of treatment-emergent adverse events qualifying as protocol-defined dose-limiting toxicities that occurred during the first month of treatment was used to determine the RP2D and/or MTD in pediatric subjects treated with tazemetostat. The ITT population included all subjects who received at least one dose of tazemetostat.

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

End point timeframe:

Cycle 1, from the start of study treatment (Day 1) until the end of the first Cycle (Day 28) of treatment

Notes:

[5] - 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: Summary statistics were provided for this study. This was a signal findings study that was not powered to make statistical comparisons.

| End point values | Overall Dose Escalation | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 46 | | | |
| Units: mg/m^2 BID | | | | |
| number (not applicable) | | | | |
| RP2D for subjects with ATRT or CNS involvement<br>RP2D for subjects without CNS involvement | 1200<br>520 | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: ORR (dose escalation only)

| End point title | ORR (dose escalation only)[6] |
|---|---|

End point description:

ORR is defined as the percentage of subjects who achieved a confirmed complete response (CR) and/or partial response (PR) defined by response evaluation criteria in solid tumors (RECIST) or response assessment in neuro-oncology (RANO) criteria from the start of tazemetostat treatment until disease progression or the start of subsequent anticancer therapy, whichever occurs first. CR is defined as disappearance of all target and non-target lesions (with all lymph nodes must be non-pathological in size or under 10 mm in short axis) and PR is defined as at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters. ORR= CR+PR. The ITT population included all subjects who received at least one dose of tazemetostat.

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

End point timeframe:

RECIST assessments performed at screening (within 14 days before start of study intervention) and every 8 weeks post start of dosing, approximately up to 302 weeks

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: There are 8 different phases in the trial (7 dose escalation phases and the dose expansion phase with 4 cohorts) within the same period (overall study). All 8 phases are encompassed within the baseline period but the dose escalation and dose expansion phases have different end points.

| End point values | Dose Escalation Level 1 | Dose Escalation Level 2 | Dose Escalation Level 3 | Dose Escalation Level 4 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 8 | 6 | 6 | 7 |
| Units: Percentage of participants | | | | |
| number (not applicable) | 0 | 0 | 0 | 14.3 |

| End point values | Dose Escalation Level 5 | Dose Escalation Level 6 | Dose Escalation Level 7 | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 6 | 6 | 7 | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 16.7 | 16.7 | 0 | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Progression Free Survival (PFS) (dose expansion only)

| End point title | Progression Free Survival (PFS) (dose expansion only)[7] |
|---|---|

End point description:

PFS was defined as the interval of time (in weeks) from the date of first dose of study drug and the earliest date of disease progression or death, from any cause defined by RECIST or RANO criteria. Disease progression is defined as at least a 20% increase in the sum of diameters of target lesions, taking as reference the smallest sum on study (including at least a 5 mm absolute increase). The presence of new lesions also constitutes to disease progression. The ITT population included all subjects who received at least one dose of tazemetostat.

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

End point timeframe:

RECIST assessments performed at screening (within 14 days before start of study intervention) and every 8 weeks post start of dosing, approximately up to 302 weeks

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: There are 8 different phases in the trial (7 dose escalation phases and the dose expansion phase with 4 cohorts) within the same period (overall study). All 8 phases are encompassed within the baseline period but the dose escalation and dose expansion phases have different end points.

| **End point values** | Dose Expansion Cohort 1 | Dose Expansion Cohort 2 | Dose Expansion Cohort 3 | Dose Expansion Cohort 4 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 19 | 20 | 18 | 6 |
| Units: weeks | | | | |
| median (confidence interval 95%) | 7.9 (6.0 to 24.3) | 7.7 (3.4 to 8.0) | 15.9 (8.0 to 21.3) | 28.3 (7.9 to 145.4) |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Overall survival (OS) (dose expansion Only)

| End point title | Overall survival (OS) (dose expansion Only)[8] |
|---|---|

End point description:

Overall survival was defined as the time (in weeks) from the first dose of study drug to the date of death due to any cause. The ITT population included all subjects who received at least one dose of tazemetostat.

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

End point timeframe:

RECIST assessments performed at screening (within 14 days before start of study intervention) and every 8 weeks post start of dosing, approximately up to 302 weeks

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: There are 8 different phases in the trial (7 dose escalation phases and the dose expansion phase with 4 cohorts) within the same period (overall study). All 8 phases are encompassed within the baseline period but the dose escalation and dose expansion phases have different end points.

| **End point values** | Dose Expansion Cohort 1 | Dose Expansion Cohort 2 | Dose Expansion Cohort 3 | Dose Expansion Cohort 4 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 19 | 20 | 18 | 6 |
| Units: weeks | | | | |
| median (confidence interval 95%) | 21.4 (11.0 to 50.3) | 14.1 (6.9 to 22.4) | 41.8 (18.6 to 55.6) | 103.1 (12.3 to 185.6) |

## Statistical analyses

No statistical analyses for this end point

## Adverse events information

Timeframe for reporting adverse events:

TEAEs:Day 1 until earlier of either 30 days after discontinuation of study treatment or until initiation of subsequent anticancer therapy, approximately 114 weeks (dose escalation phase) and 138.7 weeks (dose expansion phase). Deaths:Day 1 up to 302 weeks

Adverse event reporting additional description:

The safety population consists of all subjects in the ITT population who had at least one post-dose safety observation recorded.

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

## Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 18.0 |

## Reporting groups

| | |
|---|---|
| Reporting group title | Dose Escalation Level 1 |

Reporting group description:

Subjects with relapsed/refractory rhabdoid tumors, INI1-negative tumors, or synovial sarcoma with SS18-SSX rearrangement received oral tazemetostat 240 mg/m^2 BID in continuous 28-day cycles.

| | |
|---|---|
| Reporting group title | Dose Escalation Level 2 |

Reporting group description:

Subjects with relapsed/refractory rhabdoid tumors, INI1-negative tumors, or synovial sarcoma with SS18-SSX rearrangement received oral tazemetostat 300 mg/m^2 BID in continuous 28-day cycles.

| | |
|---|---|
| Reporting group title | Dose Escalation Level 3 |

Reporting group description:

Subjects with relapsed/refractory rhabdoid tumors, INI1-negative tumors, or synovial sarcoma with SS18-SSX rearrangement received oral tazemetostat 400 mg/m^2 BID in continuous 28-day cycles.

| | |
|---|---|
| Reporting group title | Dose Escalation Level 4 |

Reporting group description:

Subjects with relapsed/refractory rhabdoid tumors, INI1-negative tumors, or synovial sarcoma with SS18-SSX rearrangement received oral tazemetostat 520 mg/m^2 BID in continuous 28-day cycles.

| | |
|---|---|
| Reporting group title | Dose Escalation Level 5 |

Reporting group description:

Subjects with relapsed/refractory rhabdoid tumors, INI1-negative tumors, or synovial sarcoma with SS18-SSX rearrangement received oral tazemetostat 700 mg/m^2 BID in continuous 28-day cycles.

| | |
|---|---|
| Reporting group title | Dose Escalation Level 6 |

Reporting group description:

Subjects with relapsed/refractory rhabdoid tumors, INI1-negative tumors, or synovial sarcoma with SS18-SSX rearrangement received oral tazemetostat 900 mg/m^2 BID in continuous 28-day cycles.

| | |
|---|---|
| Reporting group title | Dose Escalation Level 7 |

Reporting group description:

Subjects with relapsed/refractory rhabdoid tumors, INI1-negative tumors, or synovial sarcoma with SS18-SSX rearrangement received oral tazemetostat 1200 mg/m^2 BID in continuous 28-day cycles.

| | |
|---|---|
| Reporting group title | Dose Expansion Cohort 1 |

Reporting group description:

Subjects with ATRT who participated in the dose expansion portion of the study received 1200 mg/m^2 open-label, tazemetostat BID orally in continuous 28-day cycles.

| | |
|---|---|
| Reporting group title | Dose Expansion Cohort 2 |

Reporting group description:

Subjects with MRT/ RTK/select tumors with rhabdoid features who participated in the dose expansion portion of the study. Subjects whose disease was without CNS involvement received 520 mg/m^2 open-label, tazemetostat BID orally in continuous 28-day cycles. Subjects whose disease had CNS involvement received 1200 mg/m^2 open-label, tazemetostat BID orally in continuous 28-day cycles

| | |
|---|---|
| Reporting group title | Dose Expansion Cohort 3 |

Reporting group description:

Subjects with INI-negative tumors who participated in the dose expansion portion of the study. Subjects whose disease was without CNS involvement received 520 mg/m^2 open-label, tazemetostat BID orally in continuous 28-day cycles. Subjects whose disease had CNS involvement received 1200 mg/m^2 open-label, tazemetostat BID orally in continuous 28-day cycles.

| Reporting group title | Dose Expansion Cohort 4 |
|---|---|

Reporting group description:

Subjects with one of the tumor types defined in Cohorts 1 through 3 or synovial sarcoma with SS18-SSX rearrangement received 800 mg/m^2 tazemetostat TID orally in continuous 28-day cycles.

| **Serious adverse events** | Dose Escalation Level 1 | Dose Escalation Level 2 | Dose Escalation Level 3 |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 4 / 8 (50.00%) | 1 / 6 (16.67%) | 3 / 6 (50.00%) |
| number of deaths (all causes) | 7 | 6 | 4 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Cancer pain | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Second primary malignancy | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Tumour haemorrhage | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Tumour pain | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Rhabdoid tumour | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Vascular disorders | | | |

| | | | |
|---|---|---|---|
| Superior vena cava syndrome | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Subclavian vein thrombosis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| 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 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| 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 | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Disease progression | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Hypoxia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 6 (16.67%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory failure | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Apnoea | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 6 (16.67%) | 0 / 6 (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 |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Pneumonia aspiration | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Interstitial lung disease | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Lower respiratory tract inflammation | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Lung consolidation | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Pneumonitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Pneumothorax | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Investigations | | | |
| Platelet count decreased | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Injury, poisoning and procedural complications | | | |
| Unintentional medical device removal | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Joint injury | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Nervous system disorders | | | |
| Hydrocephalus | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |

| | | | |
|---|---|---|---|
| Seizure | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Cerebrospinal fluid leakage | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Depressed level of consciousness | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Haemorrhage intracranial | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Eye disorders | | | |
| Visual impairment | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Constipation | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Intestinal obstruction | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |

| | | | |
|---|---|---|---|
| Vomiting | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Dysphagia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Melaena | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Renal and urinary disorders | | | |
| Urinary tract obstruction | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 pain | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 | | | |
| Pneumonia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Bronchitis | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Device related infection | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Influenza | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Respiratory tract infection | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Urinary tract infection | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Bacteraemia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| CNS ventriculitis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Laryngitis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Mastoid abscess | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Oral herpes | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Otitis externa | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Otitis media | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Pneumococcal bacteraemia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Respiratory syncytial virus infection | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Streptococcal bacteraemia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Tonsillitis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Vascular device infection | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Viral infection | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Vulval abscess | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Hyponatraemia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Decreased appetite | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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** | Dose Escalation Level 4 | Dose Escalation Level 5 | Dose Escalation Level 6 |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 2 / 7 (28.57%) | 3 / 6 (50.00%) | 4 / 6 (66.67%) |
| number of deaths (all causes) | 4 | 5 | 4 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Cancer pain | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Second primary malignancy | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tumour haemorrhage | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tumour pain | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Rhabdoid tumour | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Vascular disorders | | | |
| Superior vena cava syndrome | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Subclavian vein thrombosis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| 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 | | | |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 2 / 6 (33.33%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pain | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Asthenia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Disease progression | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Hypoxia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Respiratory failure | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 6 (0.00%) | 0 / 6 (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 |

| | | | |
|---|---|---|---|
| Apnoea | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| 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 aspiration | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Interstitial lung disease | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Lower respiratory tract inflammation | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Lung consolidation | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Pneumonitis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Pneumothorax | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Investigations | | | |
| Platelet count decreased | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Injury, poisoning and procedural complications | | | |
| Unintentional medical device removal | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Joint injury | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Nervous system disorders | | | |
| Hydrocephalus | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Seizure | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|---|---|---|
| Cerebrospinal fluid leakage | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Depressed level of consciousness | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Haemorrhage intracranial | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Eye disorders | | | |
| Visual impairment | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Constipation | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Intestinal obstruction | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Vomiting | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |

| | | | |
|---|---|---|---|
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Dysphagia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Melaena | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Renal and urinary disorders | | | |
| Urinary tract obstruction | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 pain | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 | | | |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 6 (16.67%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 / 7 (0.00%) | 1 / 6 (16.67%) | 0 / 6 (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 |
| Influenza | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| 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 respiratory tract infection | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumocystis jirovecii pneumonia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| 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 tract infection | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| CNS ventriculitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Laryngitis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Mastoid abscess | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Oral herpes | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Otitis externa | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Otitis media | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Pneumococcal bacteraemia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Respiratory syncytial virus infection | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Streptococcal bacteraemia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Tonsillitis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Vascular device infection | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Viral infection | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Vulval abscess | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 6 (16.67%) | 0 / 6 (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 |
| Hyponatraemia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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 |
| Decreased appetite | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (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** | Dose Escalation | Dose Expansion | Dose Expansion |
|---|---|---|---|

| | Level 7 | Cohort 1 | Cohort 2 |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 2 / 7 (28.57%) | 12 / 19 (63.16%) | 10 / 20 (50.00%) |
| number of deaths (all causes) | 7 | 15 | 18 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Cancer pain | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (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 |
| Second primary malignancy | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (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 |
| Tumour haemorrhage | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (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 |
| Tumour pain | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 1 / 20 (5.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rhabdoid tumour | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 1 / 20 (5.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Vascular disorders | | | |
| Superior vena cava syndrome | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (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 |
| Subclavian vein thrombosis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (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 |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 1 / 20 (5.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 7 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pain | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (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 |
| Asthenia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (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 |
| Disease progression | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 1 / 20 (5.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Hypoxia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 2 / 20 (10.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Respiratory failure | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 3 / 20 (15.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 3 |
| Apnoea | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (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 |

| | | | |
|---|---|---|---|
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (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 |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 1 / 20 (5.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia aspiration | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (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 |
| Interstitial lung disease | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (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 |
| Lower respiratory tract inflammation | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (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 |
| Lung consolidation | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (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 |
| Pneumonitis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (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 |
| Pneumothorax | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (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 | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 1 / 20 (5.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary haemorrhage | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (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 |
| Investigations | | | |
| Platelet count decreased | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (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 |
| Injury, poisoning and procedural complications | | | |
| Unintentional medical device removal | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (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 |
| Joint injury | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (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 |
| Nervous system disorders | | | |
| Hydrocephalus | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 4 / 19 (21.05%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 5 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Seizure | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (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 |
| Cerebrospinal fluid leakage | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (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 |

| | | | |
|---|---|---|---|
| Depressed level of consciousness | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (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 |
| Haemorrhage intracranial | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (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 |
| Eye disorders | | | |
| Visual impairment | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (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 |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (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 |
| Constipation | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 19 (0.00%) | 0 / 20 (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 |
| Intestinal obstruction | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 1 / 20 (5.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vomiting | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 2 / 19 (10.53%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (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 |

| | | | |
|---|---|---|---|
| Dysphagia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (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 |
| Melaena | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 1 / 20 (5.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Urinary tract obstruction | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (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 and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (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 pain | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (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 | | | |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 19 (0.00%) | 0 / 20 (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 | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (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 / 7 (0.00%) | 0 / 19 (0.00%) | 1 / 20 (5.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Influenza | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 2 / 19 (10.53%) | 0 / 20 (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 |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (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 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (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 |
| Respiratory tract infection | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (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 |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (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 | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (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 |
| CNS ventriculitis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (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 |
| Laryngitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (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 |
| Mastoid abscess | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (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 |
| Oral herpes | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (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 |
| Otitis externa | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Otitis media | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (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 |
| Pneumococcal bacteraemia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory syncytial virus infection | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 1 / 20 (5.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Streptococcal bacteraemia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (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 |
| Tonsillitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular device infection | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (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 |
| Viral infection | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (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 |
| Vulval abscess | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (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 |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (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 |
| Hyponatraemia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (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 |
| Decreased appetite | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 1 / 20 (5.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| **Serious adverse events** | Dose Expansion Cohort 3 | Dose Expansion Cohort 4 | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 9 / 18 (50.00%) | 3 / 6 (50.00%) | |
| number of deaths (all causes) | 16 | 4 | |
| number of deaths resulting from adverse events | 0 | 0 | |

| | | | |
|---|---|---|---|
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Cancer pain | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 6 (16.67%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Second primary malignancy | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tumour haemorrhage | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 6 (16.67%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tumour pain | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 6 (16.67%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rhabdoid tumour | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| Superior vena cava syndrome | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Subclavian vein thrombosis | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pain | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Asthenia | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Disease progression | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Hypoxia | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory failure | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Apnoea | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pleural effusion | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia aspiration | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Interstitial lung disease | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lower respiratory tract inflammation | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lung consolidation | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonitis | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumothorax | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary haemorrhage | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Investigations | | | |
| Platelet count decreased | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Unintentional medical device removal | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Joint injury | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Hydrocephalus | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 1 / 6 (16.67%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Seizure | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebrospinal fluid leakage | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Depressed level of consciousness | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Haemorrhage intracranial | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Eye disorders | | | |
| Visual impairment | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Constipation | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intestinal obstruction | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 6 (16.67%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vomiting | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dysphagia | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Melaena | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Urinary tract obstruction | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 6 (16.67%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Device related infection | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Influenza | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumocystis jirovecii pneumonia | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory tract infection | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bacteraemia | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| CNS ventriculitis | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Laryngitis | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mastoid abscess | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oral herpes | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Otitis externa | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Otitis media | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumococcal bacteraemia | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory syncytial virus infection | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Streptococcal bacteraemia | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tonsillitis | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular device infection | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Viral infection | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 6 (16.67%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vulval abscess | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyponatraemia | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Decreased appetite | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 6 (16.67%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| **Non-serious adverse events** | Dose Escalation Level 1 | Dose Escalation Level 2 | Dose Escalation Level 3 |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 8 / 8 (100.00%) | 5 / 6 (83.33%) | 6 / 6 (100.00%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Cancer pain | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |

| | | | |
|---|---|---|---|
| Tumour pain | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 6 (16.67%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 1 | 3 |
| Melanocytic naevus | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin papilloma | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Peritumoural oedema | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tumour haemorrhage | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Embolism | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hot flush | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Hypotension | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lymphoedema | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Venous thrombosis limb | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| General disorders and administration site conditions | | | |

| | | | |
|---|---|---|---|
| Fatigue | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 3 / 6 (50.00%) | 2 / 6 (33.33%) |
| occurrences (all) | 0 | 3 | 3 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 6 (16.67%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 1 | 1 |
| Oedema peripheral | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Asthenia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gait disturbance | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Catheter site swelling | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Chest pain | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Chills | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Face oedema | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Feeling cold | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Localised oedema | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Malaise | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Catheter site pain | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Influenza like illness | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Axillary pain | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Catheter site erosion | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Generalised oedema | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Peripheral swelling | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Immune system disorders | | | |
| Drug hypersensitivity | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Reproductive system and breast disorders | | | |
| Vulvovaginal rash | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Vulvovaginal pruritus | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Breast pain | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dysmenorrhoea | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Menorrhagia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Menstruation irregular | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 2 / 6 (33.33%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 4 | 1 |
| Nasal congestion | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 4 | 0 |
| Hypoxia | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 1 / 6 (16.67%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 1 | 1 |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pleural effusion | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Tachypnoea | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Atelectasis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dysphonia | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Epistaxis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 6 (16.67%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 1 | 1 |
| Productive cough | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rales | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Rhinitis allergic | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rhinorrhoea | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Interstitial lung disease | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lung consolidation | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Stridor | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Yawning | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Increased bronchial secretion | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pneumothorax | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Wheezing | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Psychiatric disorders | | | |
| Irritability | | | |
| subjects affected / exposed | 3 / 8 (37.50%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 4 | 0 | 0 |
| Insomnia | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Anxiety | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Restlessness | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Behaviour disorder | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Fear | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Agitation | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Delirium | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Depressed mood | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Depression | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Euphoric mood | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

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|---|---|---|---|
| Mental disorder | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Mental status changes | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nightmare | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Investigations | | | |
| Platelet count decreased | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 2 |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Lymphocyte count decreased | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Weight decreased | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood bromide increased | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Bacterial test positive | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 4 |
| Blood alkaline phosphatase increased | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood creatinine increased | | | |

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| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Weight increased | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| White blood cell count decreased | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Electrocardiogram QT prolonged | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| C-reactive protein increased | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| Contusion | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 0 | 1 |
| Skin laceration | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin abrasion | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ligament sprain | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Arthropod sting | | | |

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| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Fracture | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Spinal fracture | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cardiac disorders | | | |
| Sinus tachycardia | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 2 | 0 | 1 |
| Left ventricular dysfunction | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Wolff-Parkinson-White syndrome | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Defect conduction intraventricula | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sinus bradycardia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tachycardia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 2 / 6 (33.33%) | 3 / 6 (50.00%) |
| occurrences (all) | 0 | 2 | 3 |
| Dizziness | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Paraesthesia | | | |

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| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 2 | 0 | 1 |
| Dysmetria | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Auditory nerve disorder | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Facial nerve disorder | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Facial paresis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| IIIrd nerve paralysis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| IVth nerve paralysis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Lethargy | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Tremor | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 6 (16.67%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 1 | 1 |
| VIth nerve paralysis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Disturbance in attention | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Drooling | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dysgeusia | | | |

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| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dyskinesia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Haemorrhage intracranial | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hemiparesis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ataxia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyperaesthesia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Neuralgia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Neuromyopathy | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Peripheral sensory neuropathy | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Seizure | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sensory loss | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Somnolence | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| VIth nerve disorder | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 1 / 6 (16.67%) | 1 / 6 (16.67%) |
| occurrences (all) | 3 | 1 | 2 |
| Lymphopenia | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Thrombocytopenia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Leukopenia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lymphadenopathy | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Neutropenia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Neutrophilia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Leukocytosis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ear and labyrinth disorders | | | |
| Deafness | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ear discomfort | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Ear pain | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Motion sickness | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Tympanic membrane perforation | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypoacusis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| External ear inflammation | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Otorrhoea | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Deafness transitory | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Deafness unilateral | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tinnitus | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eye disorders | | | |
| Dry eye | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Eye pain | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eyelid function disorder | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

| | | | |
|---|---|---|---|
| Conjunctivitis allergic | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Corneal epithelium defect | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Exophthalmos | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gaze palsy | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Neurotrophic keratopathy | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Papilloedema | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Photophobia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrointestinal disorders | | | |
| Vomiting | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 2 / 6 (33.33%) | 3 / 6 (50.00%) |
| occurrences (all) | 1 | 3 | 5 |
| Nausea | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 2 / 6 (33.33%) | 3 / 6 (50.00%) |
| occurrences (all) | 0 | 2 | 6 |
| Constipation | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 2 / 6 (33.33%) | 3 / 6 (50.00%) |
| occurrences (all) | 1 | 2 | 4 |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Abdominal pain | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Stomatitis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Abdominal distension | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Chapped lips | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Dyspepsia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Flatulence | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Gastritis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lip blister | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Teething | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cheilitis | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dysphagia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Haemorrhoids | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Abdominal discomfort | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ascites | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Duodenal obstruction | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Haematemesis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Melaena | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Mouth ulceration | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Odynophagia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oesophagitis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tongue erythema | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tooth development disorder | | | |

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| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Toothache | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hepatobiliary disorders | | | |
| Hepatitis toxic | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cholestasis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hepatocellular injury | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyperbilirubinaemia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Jaundice | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| Dry skin | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Erythema | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pruritus | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Alopecia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blister | | | |

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| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hyperhidrosis | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Skin hyperpigmentation | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Dermatitis acneiform | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Hair texture abnormal | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Onychoclasis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash erythematous | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash macular | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash papular | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Urticaria | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dermatitis diaper | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Scab | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin lesion | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Acne | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dermatitis bullous | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dermatitis contact | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eczema | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nail disorder | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash maculo-papular | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Telangiectasia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Renal and urinary disorders | | | |
| Urinary incontinence | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Proteinuria | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urine odour abnormal | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

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|---|---|---|---|
| Acute kidney injury | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Haematuria | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nephrolithiasis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Endocrine disorders | | | |
| Hypothyroidism | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pain in extremity | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Facial asymmetry | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Myalgia | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Joint range of motion decreased | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Muscle spasms | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Muscular weakness | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Neck pain | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Bone pain | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Fracture pain | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Groin pain | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infections and infestations | | | |
| Otitis media | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rhinitis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 6 (16.67%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 1 | 1 |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oral candidiasis | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

| | | | |
|---|---|---|---|
| Candida infection | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Hordeolum | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Mucosal infection | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Otitis externa | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Otitis media acute | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pharyngitis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pharyngitis streptococcal | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Respiratory tract infection viral | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Skin infection | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Tinea pedis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Viral rash | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Conjunctivitis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Escherichia urinary tract infection | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Fungal skin infection | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Herpes simplex | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Impetigo | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Parainfluenzae virus infection | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pneumonia pneumococcal | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory syncytial virus infection | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Rhinovirus infection | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin candida | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Viral infection | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Viral rhinitis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Body tinea | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| COVID-19 | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Coronavirus infection | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Device related infection | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Enterovirus infection | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrointestinal viral infection | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Influenza | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Urinary tract infection pseudomonal | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 6 (0.00%) | 2 / 6 (33.33%) |
| occurrences (all) | 1 | 0 | 2 |
| Hypokalaemia | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 0 | 1 |
| Hypertriglyceridaemia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 2 |
| Hypophosphataemia | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hypermagnesaemia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypoalbuminaemia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 3 |
| Hyponatraemia | | | |
| subjects affected / exposed | 2 / 8 (25.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Dehydration | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyperchloraemia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyperglycaemia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Hyperkalaemia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyperuricaemia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypomagnesaemia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Hypercalcaemia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypoglycaemia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vitamin D deficiency | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypernatraemia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypocalcaemia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| **Non-serious adverse events** | Dose Escalation Level 4 | Dose Escalation Level 5 | Dose Escalation Level 6 |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 7 / 7 (100.00%) | 6 / 6 (100.00%) | 6 / 6 (100.00%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Cancer pain | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 4 | 3 | 0 |
| Tumour pain | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Melanocytic naevus | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Skin papilloma | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Peritumoural oedema | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tumour haemorrhage | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Embolism | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hot flush | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypotension | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Lymphoedema | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Venous thrombosis limb | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 2 / 6 (33.33%) | 3 / 6 (50.00%) |
| occurrences (all) | 1 | 2 | 3 |
| Pyrexia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 7 (28.57%) | 3 / 6 (50.00%) | 2 / 6 (33.33%) |
| occurrences (all) | 2 | 5 | 4 |
| Oedema peripheral | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Asthenia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gait disturbance | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Catheter site swelling | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Chest pain | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Chills | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Face oedema | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Feeling cold | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Localised oedema | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Malaise | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Catheter site pain | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Influenza like illness | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Axillary pain | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Catheter site erosion | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Generalised oedema | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Peripheral swelling | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Immune system disorders | | | |
| Drug hypersensitivity | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Reproductive system and breast disorders | | | |
| Vulvovaginal rash | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vulvovaginal pruritus | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Breast pain | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dysmenorrhoea | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Menorrhagia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Menstruation irregular | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 3 / 6 (50.00%) | 3 / 6 (50.00%) |
| occurrences (all) | 0 | 5 | 9 |
| Nasal congestion | | | |
| subjects affected / exposed | 2 / 7 (28.57%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 2 | 0 | 3 |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 2 / 6 (33.33%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Hypoxia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 0 | 1 |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tachypnoea | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Atelectasis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Dysphonia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Epistaxis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Productive cough | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Rales | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rhinitis allergic | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Rhinorrhoea | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 6 (16.67%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 1 | 2 |
| Interstitial lung disease | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lung consolidation | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Stridor | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Yawning | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Increased bronchial secretion | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pneumothorax | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Wheezing | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Psychiatric disorders | | | |

| | | | |
|---|---|---|---|
| Irritability | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Insomnia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Anxiety | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Restlessness | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Behaviour disorder | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Fear | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Agitation | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Delirium | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Depressed mood | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Depression | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Euphoric mood | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Mental disorder | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Mental status changes | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nightmare | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Investigations | | | |
| Platelet count decreased | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 6 (0.00%) | 3 / 6 (50.00%) |
| occurrences (all) | 5 | 0 | 6 |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 0 | 1 |
| Lymphocyte count decreased | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 0 | 1 |
| Weight decreased | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood bromide increased | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Bacterial test positive | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Blood alkaline phosphatase increased | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 4 | 0 | 0 |
| Blood creatinine increased | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Weight increased | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| White blood cell count decreased | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Electrocardiogram QT prolonged | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| C-reactive protein increased | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| Contusion | | | |
| subjects affected / exposed | 2 / 7 (28.57%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 4 | 0 | 0 |
| Skin laceration | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Skin abrasion | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Ligament sprain | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Arthropod sting | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Fracture | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Spinal fracture | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cardiac disorders | | | |
| Sinus tachycardia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Left ventricular dysfunction | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Wolff-Parkinson-White syndrome | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Defect conduction intraventricula | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sinus bradycardia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tachycardia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 2 / 7 (28.57%) | 2 / 6 (33.33%) | 2 / 6 (33.33%) |
| occurrences (all) | 2 | 3 | 2 |
| Dizziness | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 2 |
| Paraesthesia | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Dysmetria | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Auditory nerve disorder | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Facial nerve disorder | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Facial paresis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| IIIrd nerve paralysis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| IVth nerve paralysis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lethargy | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Tremor | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| VIth nerve paralysis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Disturbance in attention | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Drooling | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dysgeusia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dyskinesia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Haemorrhage intracranial | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hemiparesis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ataxia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyperaesthesia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Neuralgia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Neuromyopathy | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Peripheral sensory neuropathy | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Seizure | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sensory loss | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Somnolence | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| VIth nerve disorder | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood and lymphatic system disorders | | | |

| | | | |
|---|---|---|---|
| Anaemia | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 1 / 6 (16.67%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 1 | 3 |
| Lymphopenia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Thrombocytopenia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Leukopenia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lymphadenopathy | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Neutropenia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Neutrophilia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Leukocytosis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ear and labyrinth disorders | | | |
| Deafness | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Ear discomfort | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ear pain | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 0 | 3 |
| Motion sickness | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tympanic membrane perforation | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Hypoacusis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| External ear inflammation | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Otorrhoea | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Deafness transitory | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Deafness unilateral | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tinnitus | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eye disorders | | | |
| Dry eye | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eye pain | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Eyelid function disorder | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Conjunctivitis allergic | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Corneal epithelium defect | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Exophthalmos | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gaze palsy | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Neurotrophic keratopathy | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Papilloedema | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Photophobia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrointestinal disorders | | | |
| Vomiting | | | |
| subjects affected / exposed | 2 / 7 (28.57%) | 3 / 6 (50.00%) | 2 / 6 (33.33%) |
| occurrences (all) | 4 | 7 | 4 |
| Nausea | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 3 / 6 (50.00%) | 2 / 6 (33.33%) |
| occurrences (all) | 1 | 5 | 3 |
| Constipation | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 1 / 6 (16.67%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 1 | 1 |
| Diarrhoea | | | |
| subjects affected / exposed | 2 / 7 (28.57%) | 4 / 6 (66.67%) | 2 / 6 (33.33%) |
| occurrences (all) | 3 | 6 | 6 |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 3 / 6 (50.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 2 | 4 | 2 |
| Stomatitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Abdominal distension | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Chapped lips | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dyspepsia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Flatulence | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Gastritis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Lip blister | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Teething | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cheilitis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dysphagia | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Haemorrhoids | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Abdominal discomfort | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ascites | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Duodenal obstruction | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Haematemesis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Melaena | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Mouth ulceration | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Odynophagia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oesophagitis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tongue erythema | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tooth development disorder | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Toothache | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hepatobiliary disorders | | | |
| Hepatitis toxic | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Cholestasis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hepatocellular injury | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyperbilirubinaemia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Jaundice | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| Dry skin | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Erythema | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Pruritus | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Alopecia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blister | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyperhidrosis | | | |

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| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin hyperpigmentation | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Dermatitis acneiform | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hair texture abnormal | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Onychoclasis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Rash | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 0 | 1 |
| Rash erythematous | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash macular | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash papular | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urticaria | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Dermatitis diaper | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Scab | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin lesion | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Acne | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dermatitis bullous | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dermatitis contact | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eczema | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nail disorder | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash maculo-papular | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Telangiectasia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Renal and urinary disorders | | | |
| Urinary incontinence | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Proteinuria | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Urine odour abnormal | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Acute kidney injury | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Haematuria | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nephrolithiasis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Endocrine disorders | | | |
| Hypothyroidism | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Facial asymmetry | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Myalgia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Arthralgia | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Joint range of motion decreased | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Muscle spasms | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Muscular weakness | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal pain | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Neck pain | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Bone pain | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Fracture pain | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Groin pain | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infections and infestations | | | |
| Otitis media | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 1 / 6 (16.67%) | 1 / 6 (16.67%) |
| occurrences (all) | 2 | 1 | 1 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 2 / 7 (28.57%) | 1 / 6 (16.67%) | 1 / 6 (16.67%) |
| occurrences (all) | 9 | 1 | 2 |
| Rhinitis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 5 |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oral candidiasis | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Candida infection | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Hordeolum | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 2 |
| Mucosal infection | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Otitis externa | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Otitis media acute | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Pharyngitis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pharyngitis streptococcal | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Respiratory tract infection viral | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin infection | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Tinea pedis | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

| | | | |
|---|---|---|---|
| Viral rash | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Conjunctivitis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Escherichia urinary tract infection | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Fungal skin infection | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Herpes simplex | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Impetigo | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Parainfluenzae virus infection | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pneumonia pneumococcal | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory syncytial virus infection | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rhinovirus infection | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Skin candida | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Viral infection | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Viral rhinitis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Body tinea | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| COVID-19 | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Coronavirus infection | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Device related infection | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Enterovirus infection | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrointestinal viral infection | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Influenza | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urinary tract infection pseudomonal | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 3 / 7 (42.86%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 3 | 2 | 0 |
| Hypokalaemia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Hypertriglyceridaemia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypophosphataemia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 6 (16.67%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 6 | 0 |
| Hypermagnesaemia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypoalbuminaemia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyponatraemia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dehydration | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hyperchloraemia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Hyperglycaemia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyperkalaemia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 2 |
| Hyperuricaemia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Hypomagnesaemia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypercalcaemia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypoglycaemia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vitamin D deficiency | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypernatraemia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypocalcaemia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 6 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| **Non-serious adverse events** | Dose Escalation Level 7 | Dose Expansion Cohort 1 | Dose Expansion Cohort 2 |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 6 / 7 (85.71%) | 19 / 19 (100.00%) | 19 / 20 (95.00%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Cancer pain | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tumour pain | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 2 / 19 (10.53%) | 2 / 20 (10.00%) |
| occurrences (all) | 0 | 3 | 2 |
| Melanocytic naevus | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin papilloma | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Peritumoural oedema | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tumour haemorrhage | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 1 / 19 (5.26%) | 3 / 20 (15.00%) |
| occurrences (all) | 1 | 1 | 3 |
| Embolism | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hot flush | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypotension | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Lymphoedema | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Venous thrombosis limb | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 4 / 19 (21.05%) | 2 / 20 (10.00%) |
| occurrences (all) | 1 | 4 | 2 |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 4 / 19 (21.05%) | 5 / 20 (25.00%) |
| occurrences (all) | 1 | 6 | 8 |
| Oedema peripheral | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 7 (0.00%) | 2 / 19 (10.53%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 2 | 1 |
| Asthenia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 1 | 1 |
| Gait disturbance | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 2 / 19 (10.53%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Catheter site swelling | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Chest pain | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Chills | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Face oedema | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Feeling cold | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Localised oedema | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Malaise | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Catheter site pain | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Influenza like illness | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Axillary pain | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Catheter site erosion | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Generalised oedema | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Peripheral swelling | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Immune system disorders | | | |
| Drug hypersensitivity | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Reproductive system and breast disorders | | | |
| Vulvovaginal rash | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vulvovaginal pruritus | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Breast pain | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dysmenorrhoea | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Menorrhagia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Menstruation irregular | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 2 / 7 (28.57%) | 6 / 19 (31.58%) | 4 / 20 (20.00%) |
| occurrences (all) | 2 | 11 | 5 |
| Nasal congestion | | | |
| subjects affected / exposed | 2 / 7 (28.57%) | 2 / 19 (10.53%) | 1 / 20 (5.00%) |
| occurrences (all) | 2 | 2 | 1 |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 2 | 2 |
| Hypoxia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 2 / 20 (10.00%) |
| occurrences (all) | 0 | 1 | 3 |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tachypnoea | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 2 / 20 (10.00%) |
| occurrences (all) | 0 | 0 | 2 |
| Atelectasis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Dysphonia | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Epistaxis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Productive cough | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Rales | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rhinitis allergic | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 2 / 19 (10.53%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Rhinorrhoea | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Interstitial lung disease | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Lung consolidation | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Stridor | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Yawning | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Increased bronchial secretion | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Pneumothorax | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Wheezing | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Psychiatric disorders | | | |
| Irritability | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 2 / 19 (10.53%) | 1 / 20 (5.00%) |
| occurrences (all) | 2 | 2 | 1 |

| | | | |
|---|---|---|---|
| Insomnia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Anxiety | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Restlessness | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Behaviour disorder | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Fear | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Agitation | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Delirium | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Depressed mood | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Depression | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Euphoric mood | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Mental disorder | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Mental status changes | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Nightmare | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Investigations | | | |
| Platelet count decreased | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 2 / 20 (10.00%) |
| occurrences (all) | 0 | 4 | 7 |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 2 / 19 (10.53%) | 1 / 20 (5.00%) |
| occurrences (all) | 1 | 3 | 1 |
| Lymphocyte count decreased | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 2 / 19 (10.53%) | 3 / 20 (15.00%) |
| occurrences (all) | 1 | 4 | 3 |
| Weight decreased | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 3 / 20 (15.00%) |
| occurrences (all) | 0 | 1 | 3 |
| Blood bromide increased | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 2 / 19 (10.53%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 3 | 1 |
| Bacterial test positive | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 2 / 19 (10.53%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 2 | 1 |
| Blood alkaline phosphatase increased | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood creatinine increased | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 19 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 2 | 0 | 3 |
| Weight increased | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| White blood cell count decreased | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 7 (0.00%) | 2 / 19 (10.53%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Electrocardiogram QT prolonged | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| C-reactive protein increased | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Injury, poisoning and procedural complications | | | |
| Contusion | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin laceration | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Skin abrasion | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ligament sprain | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Arthropod sting | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Fracture | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Spinal fracture | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cardiac disorders | | | |
| Sinus tachycardia | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 1 / 19 (5.26%) | 2 / 20 (10.00%) |
| occurrences (all) | 2 | 1 | 2 |
| Left ventricular dysfunction | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 1 | 1 |
| Wolff-Parkinson-White syndrome | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Defect conduction intraventricula | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Sinus bradycardia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tachycardia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 2 / 20 (10.00%) |
| occurrences (all) | 0 | 0 | 2 |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 4 / 19 (21.05%) | 1 / 20 (5.00%) |
| occurrences (all) | 1 | 6 | 1 |
| Dizziness | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Paraesthesia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dysmetria | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Auditory nerve disorder | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Facial nerve disorder | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Facial paresis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| IIIrd nerve paralysis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| IVth nerve paralysis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lethargy | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tremor | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| VIth nerve paralysis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Disturbance in attention | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Drooling | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Dysgeusia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 2 | 1 |
| Dyskinesia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Haemorrhage intracranial | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Hemiparesis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Ataxia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyperaesthesia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Neuralgia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Neuromyopathy | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Peripheral sensory neuropathy | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Seizure | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Sensory loss | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Somnolence | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| VIth nerve disorder | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 2 / 7 (28.57%) | 4 / 19 (21.05%) | 8 / 20 (40.00%) |
| occurrences (all) | 4 | 29 | 18 |

| | | | |
|---|---|---|---|
| Lymphopenia | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences (all) | 3 | 1 | 0 |
| Thrombocytopenia | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences (all) | 4 | 1 | 0 |
| Leukopenia | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Lymphadenopathy | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Neutropenia | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Neutrophilia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Leukocytosis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Ear and labyrinth disorders | | | |
| Deafness | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ear discomfort | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ear pain | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Motion sickness | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tympanic membrane perforation | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypoacusis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 2 / 19 (10.53%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| External ear inflammation | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Otorrhoea | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Deafness transitory | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Deafness unilateral | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tinnitus | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eye disorders | | | |
| Dry eye | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Eye pain | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eyelid function disorder | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Conjunctivitis allergic | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Corneal epithelium defect | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

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|---|---|---|---|
| Exophthalmos | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Gaze palsy | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Neurotrophic keratopathy | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Papilloedema | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Photophobia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrointestinal disorders | | | |
| Vomiting | | | |
| subjects affected / exposed | 6 / 7 (85.71%) | 11 / 19 (57.89%) | 9 / 20 (45.00%) |
| occurrences (all) | 12 | 19 | 14 |
| Nausea | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 6 / 19 (31.58%) | 5 / 20 (25.00%) |
| occurrences (all) | 1 | 6 | 5 |
| Constipation | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 2 / 19 (10.53%) | 4 / 20 (20.00%) |
| occurrences (all) | 1 | 2 | 4 |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 7 / 19 (36.84%) | 3 / 20 (15.00%) |
| occurrences (all) | 1 | 12 | 3 |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 4 / 20 (20.00%) |
| occurrences (all) | 0 | 1 | 4 |
| Stomatitis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 1 | 1 |
| Abdominal distension | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 1 | 1 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Chapped lips | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dyspepsia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Flatulence | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Gastritis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lip blister | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Teething | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Cheilitis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Dysphagia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Haemorrhoids | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Abdominal discomfort | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ascites | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 2 / 20 (10.00%) |
| occurrences (all) | 0 | 0 | 2 |
| Duodenal obstruction | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Haematemesis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Melaena | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Mouth ulceration | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Odynophagia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oesophagitis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tongue erythema | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tooth development disorder | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Toothache | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Hepatobiliary disorders | | | |

| | | | |
|---|---|---|---|
| Hepatitis toxic | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cholestasis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Hepatocellular injury | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Hyperbilirubinaemia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Jaundice | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| Dry skin | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Erythema | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 2 / 19 (10.53%) | 2 / 20 (10.00%) |
| occurrences (all) | 1 | 2 | 2 |
| Pruritus | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 3 / 20 (15.00%) |
| occurrences (all) | 0 | 1 | 3 |
| Alopecia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Blister | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyperhidrosis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Skin hyperpigmentation | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dermatitis acneiform | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hair texture abnormal | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Onychoclasis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash erythematous | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Rash macular | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Rash papular | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urticaria | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dermatitis diaper | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 2 / 19 (10.53%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Scab | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Skin lesion | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Acne | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dermatitis bullous | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Dermatitis contact | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Eczema | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Nail disorder | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash maculo-papular | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Telangiectasia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Renal and urinary disorders | | | |
| Urinary incontinence | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Proteinuria | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Urine odour abnormal | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Acute kidney injury | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Haematuria | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Nephrolithiasis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Endocrine disorders | | | |
| Hypothyroidism | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 2 / 20 (10.00%) |
| occurrences (all) | 0 | 2 | 2 |
| Facial asymmetry | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Myalgia | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Joint range of motion decreased | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Muscle spasms | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Muscular weakness | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 19 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 2 | 0 | 1 |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Neck pain | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Bone pain | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Fracture pain | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 2 |
| Groin pain | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infections and infestations | | | |
| Otitis media | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 3 / 19 (15.79%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 2 / 19 (10.53%) | 1 / 20 (5.00%) |
| occurrences (all) | 1 | 3 | 1 |
| Rhinitis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 2 / 20 (10.00%) |
| occurrences (all) | 0 | 4 | 2 |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 2 / 20 (10.00%) |
| occurrences (all) | 0 | 1 | 2 |
| Oral candidiasis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Candida infection | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hordeolum | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Mucosal infection | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Otitis externa | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 5 | 0 |
| Otitis media acute | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pharyngitis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pharyngitis streptococcal | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 2 / 20 (10.00%) |
| occurrences (all) | 0 | 0 | 3 |
| Respiratory tract infection viral | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin infection | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Tinea pedis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Viral rash | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Conjunctivitis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Escherichia urinary tract infection | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Fungal skin infection | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Herpes simplex | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 4 | 0 |
| Impetigo | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Parainfluenzae virus infection | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pneumonia pneumococcal | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Respiratory syncytial virus infection | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Rhinovirus infection | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 1 | 1 |
| Skin candida | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

| | | | |
|---|---|---|---|
| Viral infection | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Viral rhinitis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Body tinea | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| COVID-19 | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Coronavirus infection | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Device related infection | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Enterovirus infection | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrointestinal viral infection | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Influenza | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urinary tract infection pseudomonal | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 7 (14.29%) | 5 / 19 (26.32%) | 4 / 20 (20.00%) |
| occurrences (all) | 1 | 5 | 4 |
| Hypokalaemia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 3 / 19 (15.79%) | 2 / 20 (10.00%) |
| occurrences (all) | 0 | 5 | 2 |
| Hypertriglyceridaemia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 2 / 19 (10.53%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 2 | 1 |
| Hypophosphataemia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 4 | 1 |
| Hypermagnesaemia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 2 | 1 |
| Hypoalbuminaemia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 2 / 19 (10.53%) | 2 / 20 (10.00%) |
| occurrences (all) | 0 | 4 | 2 |
| Hyponatraemia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 2 / 20 (10.00%) |
| occurrences (all) | 0 | 1 | 2 |
| Dehydration | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Hyperchloraemia | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Hyperglycaemia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyperkalaemia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Hyperuricaemia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypomagnesaemia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 7 (0.00%) | 2 / 19 (10.53%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Hypercalcaemia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 1 | 1 |
| Hypoglycaemia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Vitamin D deficiency | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 19 (5.26%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Hypernatraemia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Hypocalcaemia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 19 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| **Non-serious adverse events** | Dose Expansion Cohort 3 | Dose Expansion Cohort 4 | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 18 / 18 (100.00%) | 6 / 6 (100.00%) | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Cancer pain | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Tumour pain | | | |
| subjects affected / exposed | 3 / 18 (16.67%) | 0 / 6 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Melanocytic naevus | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Skin papilloma | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Peritumoural oedema | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Tumour haemorrhage | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 2 | |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 2 / 18 (11.11%) | 1 / 6 (16.67%) | |
| occurrences (all) | 3 | 3 | |
| Embolism | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Hot flush | | | |
| subjects affected / exposed | 2 / 18 (11.11%) | 0 / 6 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Hypotension | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Lymphoedema | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Venous thrombosis limb | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 5 / 18 (27.78%) | 2 / 6 (33.33%) | |
| occurrences (all) | 7 | 3 | |
| Pyrexia | | | |
| subjects affected / exposed | 7 / 18 (38.89%) | 0 / 6 (0.00%) | |
| occurrences (all) | 16 | 0 | |
| Oedema peripheral | | | |
| subjects affected / exposed | 5 / 18 (27.78%) | 0 / 6 (0.00%) | |
| occurrences (all) | 6 | 0 | |
| Asthenia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 18 (5.56%) | 3 / 6 (50.00%) | |
| occurrences (all) | 1 | 3 | |
| Gait disturbance | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| Catheter site swelling | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Chest pain | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 1 / 6 (16.67%) | |
| occurrences (all) | 1 | 1 | |
| Chills | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Face oedema | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Feeling cold | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Localised oedema | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Malaise | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 1 / 6 (16.67%) | |
| occurrences (all) | 1 | 1 | |
| Catheter site pain | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Influenza like illness | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Axillary pain | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| Catheter site erosion | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Generalised oedema | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Peripheral swelling | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| Immune system disorders | | | |
| Drug hypersensitivity | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Reproductive system and breast disorders | | | |
| Vulvovaginal rash | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Vulvovaginal pruritus | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Breast pain | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Dysmenorrhoea | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| Menorrhagia | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Menstruation irregular | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 1 / 6 (16.67%) | |
| occurrences (all) | 1 | 2 | |
| Respiratory, thoracic and mediastinal disorders | | | |

| | | | |
|---|---|---|---|
| Cough | | | |
| subjects affected / exposed | 6 / 18 (33.33%) | 3 / 6 (50.00%) | |
| occurrences (all) | 8 | 4 | |
| Nasal congestion | | | |
| subjects affected / exposed | 2 / 18 (11.11%) | 0 / 6 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 3 / 6 (50.00%) | |
| occurrences (all) | 0 | 4 | |
| Hypoxia | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 3 / 18 (16.67%) | 1 / 6 (16.67%) | |
| occurrences (all) | 4 | 1 | |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| Tachypnoea | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Atelectasis | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Dysphonia | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Epistaxis | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Productive cough | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Rales | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |

| | | | |
|---|---|---|---|
| Rhinitis allergic | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Rhinorrhoea | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Interstitial lung disease | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Lung consolidation | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Stridor | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Yawning | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Increased bronchial secretion | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Pneumothorax | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| Wheezing | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Psychiatric disorders | | | |
| Irritability | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Insomnia | | | |
| subjects affected / exposed | 3 / 18 (16.67%) | 1 / 6 (16.67%) | |
| occurrences (all) | 3 | 1 | |
| Anxiety | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 18 (11.11%) | 0 / 6 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Restlessness | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Behaviour disorder | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Fear | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Agitation | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Delirium | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Depressed mood | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| Depression | | | |
| subjects affected / exposed | 2 / 18 (11.11%) | 0 / 6 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Euphoric mood | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Mental disorder | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Mental status changes | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| Nightmare | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Investigations | | | |

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|---|---|---|---|---|
| Platelet count decreased | | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | | |
| occurrences (all) | 0 | 0 | | |
| Aspartate aminotransferase increased | | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 6 (16.67%) | | |
| occurrences (all) | 0 | 1 | | |
| Lymphocyte count decreased | | | | |
| subjects affected / exposed | 2 / 18 (11.11%) | 0 / 6 (0.00%) | | |
| occurrences (all) | 2 | 0 | | |
| Weight decreased | | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 2 / 6 (33.33%) | | |
| occurrences (all) | 0 | 8 | | |
| Blood bromide increased | | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 1 / 6 (16.67%) | | |
| occurrences (all) | 1 | 2 | | |
| Bacterial test positive | | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | | |
| occurrences (all) | 0 | 0 | | |
| Alanine aminotransferase increased | | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | | |
| occurrences (all) | 0 | 0 | | |
| Blood alkaline phosphatase increased | | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | | |
| occurrences (all) | 2 | 0 | | |
| Blood creatinine increased | | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 6 (16.67%) | | |
| occurrences (all) | 0 | 2 | | |
| Weight increased | | | | |
| subjects affected / exposed | 2 / 18 (11.11%) | 0 / 6 (0.00%) | | |
| occurrences (all) | 2 | 0 | | |
| White blood cell count decreased | | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | | |
| occurrences (all) | 1 | 0 | | |
| Electrocardiogram QT prolonged | | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| C-reactive protein increased | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Injury, poisoning and procedural complications | | | |
| Contusion | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Skin laceration | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Skin abrasion | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Ligament sprain | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Arthropod sting | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Fracture | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Spinal fracture | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Cardiac disorders | | | |

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|---|---|---|---|
| Sinus tachycardia | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 1 / 6 (16.67%) | |
| occurrences (all) | 1 | 2 | |
| Left ventricular dysfunction | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Wolff-Parkinson-White syndrome | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Defect conduction intraventricula | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Sinus bradycardia | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Tachycardia | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 7 / 18 (38.89%) | 3 / 6 (50.00%) | |
| occurrences (all) | 9 | 3 | |
| Dizziness | | | |
| subjects affected / exposed | 2 / 18 (11.11%) | 1 / 6 (16.67%) | |
| occurrences (all) | 2 | 2 | |
| Paraesthesia | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Dysmetria | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Auditory nerve disorder | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Facial nerve disorder | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Facial paresis | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| IIIrd nerve paralysis | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| IVth nerve paralysis | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Lethargy | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Tremor | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 1 / 6 (16.67%) | |
| occurrences (all) | 1 | 1 | |
| VIth nerve paralysis | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Disturbance in attention | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Drooling | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Dysgeusia | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| Dyskinesia | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 1 / 6 (16.67%) | |
| occurrences (all) | 1 | 1 | |
| Haemorrhage intracranial | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Hemiparesis | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Ataxia | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| Hyperaesthesia | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Neuralgia | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Neuromyopathy | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| Peripheral sensory neuropathy | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Seizure | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Sensory loss | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Somnolence | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| VIth nerve disorder | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 5 / 18 (27.78%) | 0 / 6 (0.00%) | |
| occurrences (all) | 13 | 0 | |
| Lymphopenia | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 3 / 6 (50.00%) | |
| occurrences (all) | 0 | 10 | |

| | | | |
|---|---|---|---|
| Thrombocytopenia | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 2 / 6 (33.33%) | |
| occurrences (all) | 1 | 7 | |
| Leukopenia | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| Lymphadenopathy | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Neutropenia | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Neutrophilia | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Leukocytosis | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Ear and labyrinth disorders | | | |
| Deafness | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Ear discomfort | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Ear pain | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Motion sickness | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Tympanic membrane perforation | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Hypoacusis | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| External ear inflammation | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Otorrhoea | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Deafness transitory | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Deafness unilateral | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Tinnitus | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Eye disorders | | | |
| Dry eye | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Eye pain | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Eyelid function disorder | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Conjunctivitis allergic | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Corneal epithelium defect | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Exophthalmos | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |

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|---|---|---|---|
| Gaze palsy | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Neurotrophic keratopathy | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Papilloedema | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| Photophobia | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Gastrointestinal disorders | | | |
| Vomiting | | | |
| subjects affected / exposed | 11 / 18 (61.11%) | 5 / 6 (83.33%) | |
| occurrences (all) | 34 | 19 | |
| Nausea | | | |
| subjects affected / exposed | 11 / 18 (61.11%) | 3 / 6 (50.00%) | |
| occurrences (all) | 16 | 3 | |
| Constipation | | | |
| subjects affected / exposed | 3 / 18 (16.67%) | 2 / 6 (33.33%) | |
| occurrences (all) | 3 | 2 | |
| Diarrhoea | | | |
| subjects affected / exposed | 7 / 18 (38.89%) | 2 / 6 (33.33%) | |
| occurrences (all) | 11 | 4 | |
| Abdominal pain | | | |
| subjects affected / exposed | 3 / 18 (16.67%) | 1 / 6 (16.67%) | |
| occurrences (all) | 6 | 1 | |
| Stomatitis | | | |
| subjects affected / exposed | 3 / 18 (16.67%) | 0 / 6 (0.00%) | |
| occurrences (all) | 4 | 0 | |
| Abdominal distension | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Abdominal pain upper | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| Chapped lips | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Dyspepsia | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Flatulence | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Gastritis | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Lip blister | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Teething | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Cheilitis | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Dysphagia | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Haemorrhoids | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Abdominal discomfort | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| Ascites | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Duodenal obstruction | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Haematemesis | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Melaena | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Mouth ulceration | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Odynophagia | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Oesophagitis | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Tongue erythema | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Tooth development disorder | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Toothache | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| Hepatobiliary disorders | | | |
| Hepatitis toxic | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |

| | | | |
|---|---|---|---|
| Cholestasis | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Hepatocellular injury | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Hyperbilirubinaemia | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Jaundice | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| Skin and subcutaneous tissue disorders | | | |
| Dry skin | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| Erythema | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Pruritus | | | |
| subjects affected / exposed | 2 / 18 (11.11%) | 0 / 6 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Alopecia | | | |
| subjects affected / exposed | 3 / 18 (16.67%) | 1 / 6 (16.67%) | |
| occurrences (all) | 3 | 1 | |
| Blister | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Hyperhidrosis | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Skin hyperpigmentation | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Dermatitis acneiform | | | |

| | | | | |
|---|---|---|---|---|
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | | |
| occurrences (all) | 2 | 0 | | |
| Hair texture abnormal | | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | | |
| occurrences (all) | 0 | 0 | | |
| Onychoclasis | | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | | |
| occurrences (all) | 0 | 0 | | |
| Rash | | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | | |
| occurrences (all) | 1 | 0 | | |
| Rash erythematous | | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | | |
| occurrences (all) | 0 | 0 | | |
| Rash macular | | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | | |
| occurrences (all) | 0 | 0 | | |
| Rash papular | | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | | |
| occurrences (all) | 0 | 0 | | |
| Urticaria | | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | | |
| occurrences (all) | 4 | 0 | | |
| Dermatitis diaper | | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | | |
| occurrences (all) | 0 | 0 | | |
| Scab | | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | | |
| occurrences (all) | 0 | 0 | | |
| Skin lesion | | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | | |
| occurrences (all) | 0 | 0 | | |
| Acne | | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | | |
| occurrences (all) | 1 | 0 | | |
| Dermatitis bullous | | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Dermatitis contact | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Eczema | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Nail disorder | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| Rash maculo-papular | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Telangiectasia | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Renal and urinary disorders | | | |
| Urinary incontinence | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Proteinuria | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Urine odour abnormal | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Acute kidney injury | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| Haematuria | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 2 / 6 (33.33%) | |
| occurrences (all) | 0 | 2 | |
| Nephrolithiasis | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |

| | | | |
|---|---|---|---|
| Endocrine disorders | | | |
| Hypothyroidism | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 4 / 18 (22.22%) | 2 / 6 (33.33%) | |
| occurrences (all) | 4 | 2 | |
| Pain in extremity | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 1 / 6 (16.67%) | |
| occurrences (all) | 1 | 1 | |
| Facial asymmetry | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Myalgia | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| Joint range of motion decreased | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Muscle spasms | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Muscular weakness | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 1 / 6 (16.67%) | |
| occurrences (all) | 1 | 1 | |
| Neck pain | | | |
| subjects affected / exposed | 2 / 18 (11.11%) | 0 / 6 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Bone pain | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| Fracture pain | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Groin pain | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Infections and infestations | | | |
| Otitis media | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 3 / 18 (16.67%) | 0 / 6 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Rhinitis | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 1 / 6 (16.67%) | |
| occurrences (all) | 2 | 1 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Oral candidiasis | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Candida infection | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Hordeolum | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |

| | | | |
|---|---|---|---|
| Mucosal infection | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Otitis externa | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Otitis media acute | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Pharyngitis | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Pharyngitis streptococcal | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Respiratory tract infection viral | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Sinusitis | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Skin infection | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Tinea pedis | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Viral rash | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |

| | | | |
|---|---|---|---|
| Conjunctivitis | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| Escherichia urinary tract infection | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Fungal skin infection | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Herpes simplex | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Impetigo | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 1 / 6 (16.67%) | |
| occurrences (all) | 1 | 1 | |
| Parainfluenzae virus infection | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Pneumonia pneumococcal | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Respiratory syncytial virus infection | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Rhinovirus infection | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Skin candida | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Viral infection | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |

| | | | |
|---|---|---|---|
| Viral rhinitis | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Body tinea | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| COVID-19 | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Coronavirus infection | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Device related infection | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Enterovirus infection | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Gastroenteritis | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Gastrointestinal viral infection | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Influenza | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| Urinary tract infection pseudomonal | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 4 / 18 (22.22%) | 1 / 6 (16.67%) | |
| occurrences (all) | 4 | 1 | |
| Hypokalaemia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 2 | |
| Hypertriglyceridaemia | | | |
| subjects affected / exposed | 2 / 18 (11.11%) | 0 / 6 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Hypophosphataemia | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 2 / 6 (33.33%) | |
| occurrences (all) | 1 | 2 | |
| Hypermagnesaemia | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 1 / 6 (16.67%) | |
| occurrences (all) | 1 | 1 | |
| Hypoalbuminaemia | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Hyponatraemia | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| Hyperchloraemia | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Hyperkalaemia | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Hyperuricaemia | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Hypomagnesaemia | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| Hypercalcaemia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Hypoglycaemia | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Vitamin D deficiency | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Hypernatraemia | | | |
| subjects affected / exposed | 0 / 18 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Hypocalcaemia | | | |
| subjects affected / exposed | 1 / 18 (5.56%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 13 July 2015 | Original Protocol submitted to FDA, never submitted to sites. |
| 24 August 2015 | Amendment v1.0 – submitted to all sites.<br>Key changes:<br>- Added a dose level to start at a lower dose (240mg/m2 vs. original 300mg/m2) and effectively increasing the dose escalation phase numbers from 18 to 24 subjects.<br>- Additional details on blood sampling volumes added.<br>- Removed mandatory requirement to collect date of birth. |
| 02 October 2015 | Amendment v2.0 – submitted to all sites.<br>Key changes:<br>- Added selected tumors with rhabdoid features that responses were seen in Phase 1 (SMARCA4 loss in MRTO or SCCOHT).<br>- Removed requirement for fasting based upon data in food-effect study.<br>- Removed restriction for pregnancy prevention 30 days prior to entry. |
| 12 October 2015 | Amendment v2.1 – Country-specific for Germany<br>Key changes:<br>- Upper age limit changes to <12 years old due to inability to do Panorex films in Germany (radiation exposure an issue).<br>- Removed MUGA scan as it is not performed in Germany.<br>- Removed bone monitoring and Karnofsky performance due to age change. |
| 03 December 2015 | Amendment v2.2 – Country-specific for United Kingdom<br>Key changes:<br>- Lower age limit increased to >1 year old (vs. 6 mos for rest of world).<br>- No subjects <5 years old in UK will be enrolled until 4 subjects study wide have received at least 4 weeks of study drug.<br>- Pregnancy prevention in females and males updated to reflect UK law. |
| 31 March 2016 | Amendment v2.3 – Country-specific for Germany<br>Key changes:<br>- Removal of synovial and other INI1-negative/SMARCA4 negative tumors |
| 11 May 2016 | Amendment v3.0 – submitted to all sites.<br>Key changes:<br>- Changes to include treated brain mets.<br>- Remove Panorex.<br>- Remove baseline visit and other changes made to 202.<br>- Add cohorts - Cohort 1: atypical teratoid rhabdoid tumor (ATRT), Cohort 2: non-ATRT rhabdoid tumors and Cohort 3: INI1-negative tumors or synovial sarcoma. |
| 22 June 2016 | Amendment v3.1 – Country-specific for Germany<br>Key changes:<br>- Incorporating all changes from amendment v3.0 |

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|---|---|
| 13 July 2016 | Amendment v3.2 – Country-specific for United Kingdom<br>Key changes:<br>- Incorporating all changes from amendment v3.0 |
| 27 July 2016 | Amendment v4.0 – submitted to all sites<br>Key changes:<br>- Four dose expansion levels added.<br>- Number of subjects changed from 84 to 108.<br>- Allow replacement of subjects who discontinue in absence of a dose-limiting toxicity [DLT] prior to the completing of the DLT evaluation period. |
| 02 August 2016 | Amendment v4.1 – Country-specific for Germany<br>Key changes:<br>- All changes from v4.0 incorporated |
| 21 October 2016 | Amendment v4.3 – Country-specific for United Kingdom<br>Key changes:<br>- All changes from v4.0 incorporated |
| 20 July 2017 | Amendment v5.0 – submitted to all sites<br>Key changes:<br>- RP2D was determined to be 1200 mg/m2 BID and will be used in the dose expansion portion of the study.<br>- New cohort 4 added for subjects ≥10 years to ≤21 years to receive tazemetostat tablets.<br>- Number of subjects changed from 108 to 120.<br>- Information on hydrobromide salt, hyperchloremia and potential associated toxicities added.<br>- Cycle length and study procedure timings changed for Cycles 13 and beyond to 21 days. |
| 26 July 2017 | Amendment v5.3 – Country-specific for United Kingdom<br>Key changes:<br>- Tablet formulation cohort added; this cohort (Cohort 4) will not enroll subjects in Germany<br>- The RP2D was determined to be 1200 mg/m2 BID and will be the dose used in the dose expansion portion of the study<br>- New cohort added to Dose Expansion phase of study (outside of Germany): Cohort 4 to received tazemetostat tablets 800 mg/m2 TID [2400 mg/m2/day]); Subjects are to be ≥10 years to ≤21 years with one of the tumor types defined in Cohorts 1 through 3 or synovial sarcoma with SS18-SSX rearrangement and able to swallow tablets)<br>- Information on hydrobromide salt, hyperchloremia, and potential associated toxicities had been added; also, bromide measurements have been added<br>- Number of subjects increased from 108 to 120<br>- Additional preliminary PK data added<br>- Additional prohibited medications added<br>- Cycle length for Cycles 13 and beyond changed to 21 days.<br>- Study procedure timings updated for Cycles 13 and beyond to reflect 21-day cycle<br>- Dose modification information has been updated<br>- Expansion of requirements for additional biopsies for subjects who progress to include all subjects (including SD) not just subjects who experienced PR or better.<br>- Safety section has been updated<br>- New appendix added for Cohort 4 dosing and dose modification<br>- Minor corrections |

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|---|---|
| 03 August 2017 | Amendment v5.1 – Country-specific for Germany<br>Key changes:<br>- Tablet formulation cohort added; this cohort (Cohort 4) will not enroll subjects in Germany<br>- The RP2D was determined to be 1200 mg/m2 BID and will be the dose used in the dose expansion portion of the study<br>- New cohort added to Dose Expansion phase of study (outside of Germany): Cohort 4 to received tazemetostat tablets 800 mg/m2 TID [2400 mg/m2/day]); Subjects are to be ≥10 years to ≤21 years with one of the tumor types defined in Cohorts 1 through 3 or synovial sarcoma with SS18-SSX rearrangement and able to swallow tablets)<br>- Information on hydrobromide salt, hyperchloremia, and potential associated toxicities had been added; also, bromide measurements have been added<br>- Number of subjects increased from 108 to 120<br>- Additional preliminary PK data added<br>- Additional prohibited medications added<br>- Cycle length for Cycles 13 and beyond changed to 21 days.<br>- Study procedure timings updated for Cycles 13 and beyond to reflect 21-day cycle<br>- Dose modification information has been updated<br>- Expansion of requirements for additional biopsies for subjects who progress to include all subjects (including SD) not just subjects who experienced PR or better.<br>- Safety section has been updated<br>- New appendix added for Cohort 4 dosing and dose modification<br>- Minor corrections |
| 31 October 2017 | Amendment v5.4 – Country-specific for France<br>Key changes:<br>- Updated text on phototoxicity.<br>- Updated text to clarify chloride levels are assessed at every visit locally and centrally and bromide levels will be analyzed centrally.<br>- Added additional prohibited meds.<br>- Removed PD samples at C13 and beyond.<br>- Correct inconsistency in Exclusion criteria #11 in two different sections of the protocol.<br>- Remove PD blood sample collection from procedures and assessments conducted at Cycle 13 and beyond. Add language about stopping PD sample collection after 20 evaluable PD samples are collected through Day 15 upon Sponsor notification.<br>- Minor corrections |
| 01 February 2018 | Amendment v5.5 – Country-specific for France<br>Key changes:<br>- Option to change from suspension to tablets |
| 28 September 2018 | Amendment v6.0 – submitted to all sites<br>Key changes:<br>- All changes from v5.5<br>- Updated with 2 new AESIs – T-LBL/T-ALL and MDS.<br>- Added exclusion criteria to exclude patients with thrombocytopenia, neutropenia, anemia of Grade ≥3 and history of MDS and T-LBL and MDS.<br>- Hold treatment to either modify or discontinue if patient develop MDS/AML.<br>- Patients have a maximum of cumulative 2 years on the study.<br>- Updated dose modification or discontinuation section.<br>- Changed age from ≤21 years to <18 years.<br>- Addition of assessments – blood smear morphology and annual PK.<br>- Removed Cycle 13 and beyond study design.<br>- Allow patients to change to tablet dosing after completion of Cycle 1 |

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| 10 October 2018 | Amendment v6.2 – Country-specific for United Kingdom<br>- All changes from v6.0 incorporated |
| 07 November 2018 | Amendment v6.1 – Country-specific for Germany<br>- All changes from v6.0 incorporated |
| 13 December 2018 | Amendment v7.2 – Country-specific for United Kingdom<br>- All changes from v7.0 incorporated |
| 17 December 2018 | Amendment v7.0 – submitted to all sites.<br>Key changes:<br>- Addition of the option to discontinue treatment if the Investigator determines the dose of tazemetostat must be modified for subjects enrolled in the dose expansion part of the study.<br>- Alignment of the disease assessment frequency of bone scans with the RECIST guidelines in Appendix 4.<br>- Update of dose rationale language with the starting dose of 520 mg/m2 BID for newly enrolled subjects with non-ATRT tumors to align with the new dosing requirements.<br>- Cohort 1 enrollment has been closed as there has been sufficient data collected in pediatric subjects with ATRT.<br>- Cohort 4 enrollment has been closed as there has been sufficient pharmacokinetic data collected in pediatric subjects who were administered tazemetostat in tablet form.<br>- Removal of language allowing subjects who do not have clinical or radiographic disease progression and do not experience unacceptable toxicity to receive tazemetostat beyond cycle 1. Removal of language allowing subjects who have modest disease progression in the absence of clinical deterioration to remain on study.<br>- Addition of the definition of adverse drug reaction to the overall definitions section.<br>- Addition of the definition of a suspected unexpected serious adverse reaction (SUSAR) to the overall definitions section.<br>- Addition of safety language to suggest that rapid communication of adverse events of special interest should be communicated to the Sponsor to allow the event to be understood and characterized in a timely manner.<br>- Removal of dose escalation from interim analysis section of the statistical analysis plan, as this was added in error.<br>- Change in the confidence interval from 90% to 95% when calculating overall survival, and from 80% to 95% when calculating objective response rate. |
| 15 March 2019 | Amendment v6.3 – Country-specific for Germany<br>Key changes:<br>- Removal of the option of tablet dosing as dose reduction, if needed, is not possible with the tablet formulations currently in use.<br>- Removal of the requirement of Karnofsky Performance Status >50% for subjects ≥12 years of age as all subjects in Germany are <12 years of age upon enrollment, and the Lansky Performance Scale is used for subjects <12 years of age.<br>- Removal of the requirement specific to French subjects, that they be affiliated with or a beneficiary or a social security category, as this protocol only applies to subjects in Germany.<br>- Removal of the requirement of SMARCA4 loss from IHC or molecular confirmation of SMARCA4 loss as this gene is associated with SCCOHT tumors, which will not be studied in Germany.<br>- Removal of the requirement for subjects enrolled in cohort 4 (not open in Germany) to be able to swallow tablets as tablet dosing options will no longer be permitted.<br>- Removal of language stating that for subjects who have modest disease progression in the absence of clinical deterioration and are receiving clinical benefit in the opinion of the Investigator, the Investigator should contact the Medical Monitor to discuss keeping the subject on study as subjects must come off study in the event of disease progression. |

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|---|---|
| 20 February 2020 | Amendment v8.0 – submitted to all sites.<br>Key changes:<br>- Updated the study period to reflect the first subject's first visit and current projections for last subject last visit.<br>- Updated the anticipated safety profile to align with the current IB.<br>- Included T-LBL/T-ALL with other events that will trigger convening of safety committees and to clarify that consequences of an event of T-LBL/T-ALL will occur regardless of dose level.<br>- Modified dose modification text to state that for MDS, AML or any myeloid malignancy like MPN, tazemetostat will be discontinued.<br>- Removed dose modification sub-section for dose modifications due to MDS.<br>- Adjusted and clarified dose modifications for subjects in dose expansion starting at 1200mg/m2 and for subjects starting at 520mg/m2.<br>- Removed blood chemistry collection at Day 15 of Cycles 2 and beyond to reduce the amount of blood drawn for unnecessary testing.<br>- Modified requirement for the timing of screening disease assessments to allow for assessments done more than 14 days before enrollment.<br>- Updated contraception requirements to reflect current expectations and to align with approved labeling in the US.<br>- Added genitourinary exam to comprehensive physical exam to ensure abnormalities and malignancies are not missed.<br>- Specified that elevated bromide is considered an event of clinical interest, and that events of clinical interest are to be reported in the same manner as SAEs.<br>- Corrected the confidence internal from 90% to 95% to be estimated in the case of sufficient number of deaths to trigger survival endpoint assessments by Brookneyer-Crowley. |
| 03 April 2020 | Amendment v8.2 – Country-specific for United Kingdom<br>- All changed from v8.0 incorporated |
| 03 April 2020 | Amendment v8.3 – Country-specific for Germany<br>- All changed from v8.0 incorporated |
| 01 July 2020 | Amendment v8.4 – Country-specific for Germany<br>Key changes:<br>- Clarification of the roles of existing safety committees.<br>- Corrected an inaccuracy in wording that was made to clarify that if enrollment of new patients is suspended in the event of a new case of T-LBL/T-ALL, patients on study who continue to derive clinical benefit "may" (rather than "will") be maintained on therapy. |

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? Yes

| Date | Interruption | Restart date |
|---|---|---|

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| 06 April 2018 | On 06 April 2018, an event of T-LBL was observed in a pediatric subject on study EZH-102.<br><br>The SUSAR of T-LBL resulted in the Sponsor initiating a temporary global halt in enrollment for the pediatric study EZH-102. In addition, this event led to a partial clinical hold (PCH) on new subject enrollment for tazemetostat by the U.S. (FDA), France (ANSM), and Germany (BfArM) across all studies of the Tazemetostat Development Program.<br><br>Following this report, Epizyme conducted a comprehensive evaluation. Based on this evaluation, we continued to believe that tazemetostat is a clinically active drug and has the potential to benefit both adult and pediatric patients across different tumor types where there are unmet medical needs. We also concluded that the risk assessment identifies a possible direct association between tazemetostat and T-LBL/T-ALL. Epizyme considers the risk for T-LBL/T-ALL in tazemetostat clinical trials to be largely concentrated in pediatric patients based on 1) higher AUC0-24h exposures in pediatric patients, 2) increases over time in age-related thymic involution, and 3) the known epidemiology/pathophysiology of T-LBL/ALL. The risk of T-LBL/T-ALL in adults is not known, however the incidence of treatment-related T-LBL/T-ALL in adults is expected to be uncommon.<br><br>Heightened surveillance was and continues to be conducted to monitor and identify early signs and symptoms (per local practice/standard of care) of T-LBL/T-ALL so that tazemetostat may be discontinued in the subject and treatment can be initiated for these malignancies. If a case of adult T-LBL/T-ALL occurs, enrollment will be suspended and the benefit-risk of the drug will be assessed by the Tazemetostat Safety Committee and will be communicated to all Health Authorities and Ethics Committees.<br>To date, no adult T-LBL/T-ALL cases have occurred. | 28 September 2018 |

Notes:

## Limitations and caveats

None reported