# Clinical trial results:
# An Open-Label Extension Study for Patients With Spinal Muscular Atrophy Who Previously Participated in Investigational Studies of ISIS 396443

## Summary

| | |
|---|---|
| EudraCT number | 2015-001870-16 |
| Trial protocol | DE GB SE ES FR BE IT |
| Global end of trial date | 21 August 2023 |

### Results information

| | |
|---|---|
| Result version number | v2 (current) |
| This version publication date | 30 November 2024 |
| First version publication date | 08 March 2024 |
| Version creation reason | • Correction of full data set<br>Updates to the endpoints section after resolving CTg results. |

## Trial information

### Trial identification

| | |
|---|---|
| Sponsor protocol code | ISIS 396443-CS11 |

### Additional study identifiers

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02594124 |
| WHO universal trial number (UTN) | - |

Notes:

### Sponsors

| | |
|---|---|
| Sponsor organisation name | Biogen |
| Sponsor organisation address | 250 Binney Street, Cambridge, Massachusetts, United States, 02142 |
| Public contact | Study Medical Director, Biogen, clinicaltrials@biogen.com |
| Scientific contact | Study Medical Director, Biogen, clinicaltrials@biogen.com |

Notes:

### Paediatric regulatory details

| | |
|---|---|
| Is trial part of an agreed paediatric investigation plan (PIP) | Yes |
| EMA paediatric investigation plan number(s) | EMEA-001448-PIP01-13 |
| 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? | Yes |

Notes:

## Results analysis stage

| | |
|---|---|
| Analysis stage | Final |
| Date of interim/final analysis | 21 August 2023 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 21 August 2023 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

The primary objective of the trial is to evaluate the long-term safety and tolerability of nusinersen (ISIS 396443) administered by intrathecal (IT) injection to participants with spinal muscular atrophy (SMA) who previously participated in investigational studies of ISIS 396443.

Protection of trial subjects:

Written informed consent was obtained from each subject’s parent or legal guardian prior to evaluations being performed for eligibility. Adequate time to review the information in the informed consent and ask questions concerning all portions of the conduct of the study was provided. Through the informed consent process, awareness of the purpose of the study, the procedures, the benefits and risks of the study, the discomforts and the precautions taken was made. Any side effects or other health issues occurring during the study were followed up by the study doctor. Subjects were able to stop taking part in the study at any time without giving any reason.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 04 November 2015 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | United States: 177 |
| Country: Number of subjects enrolled | Italy: 25 |
| Country: Number of subjects enrolled | Germany: 23 |
| Country: Number of subjects enrolled | Spain: 15 |
| Country: Number of subjects enrolled | Japan: 11 |
| Country: Number of subjects enrolled | Canada: 8 |
| Country: Number of subjects enrolled | France: 7 |
| Country: Number of subjects enrolled | Korea, Republic of: 5 |
| Country: Number of subjects enrolled | Sweden: 5 |
| Country: Number of subjects enrolled | Türkiye: 5 |
| Country: Number of subjects enrolled | Australia: 4 |
| Country: Number of subjects enrolled | United Kingdom: 3 |
| Country: Number of subjects enrolled | Hong Kong: 3 |
| Country: Number of subjects enrolled | Belgium: 1 |
| Worldwide total number of subjects | 292 |
| EEA total number of subjects | 76 |

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) | 89 |
| Children (2-11 years) | 187 |
| Adolescents (12-17 years) | 12 |
| Adults (18-64 years) | 4 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

Participants were enrolled at investigative sites in Australia, Belgium, Canada, Germany, Spain, France, United Kingdom, Hong Kong, Italy, Japan, Republic of Korea, Sweden, Turkey, and the United States from 04 November 2015 to 21 August 2023.

### Pre-assignment

Screening details:

A total of 292 participants with infantile and later onset spinal muscular atrophy (SMA) who previously participated in ISIS 396443-CS3B[NCT02193074], ISIS 396443-CS4[NCT02292537], ISIS 396443-CS3A[NCT01839656], ISIS 396443-CS12[NCT02052791] and 232SM202[NCT02462759] were enrolled and treated in Modified Maintenance Dosing Regimen (MMDR) period.

### 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** | Infantile SMA Onset CS3A |

Arm description:

Participants who received nusinersen in study ISIS 396443-CS3A, in an open-label period, received maintenance doses of nusinersen, intrathecal (IT) injection, on days 1, 120, 240, 360, 480, 600, 720, 840, 960, 1080, 1200, 1320, 1440, 1560, and 1680 in MMDR period of this study.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Nusinersen |
| Investigational medicinal product code | |
| Other name | ISIS 396443 |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intrathecal use |

Dosage and administration details:

Administered as specified in the treatment arm.

| | |
|---|---|
| **Arm title** | Infantile SMA Onset CS3B Previous Control |

Arm description:

Participants who received sham procedures in study ISIS 396443-CS3B, in a double-blind period, received 4 loading doses of nusinersen IT injection on Days 1, 15, 29, and 64 followed by maintenance doses of nusinersen IT injection, on days 1, 120, 240, 360, 480, 600, 720, 840, 960, 1080, 1200, 1320, 1440, 1560, and 1680 in MMDR period of this study.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Nusinersen |
| Investigational medicinal product code | |
| Other name | ISIS 396443 |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intrathecal use |

Dosage and administration details:

Administered as specified in the treatment arm.

| | |
|---|---|
| **Arm title** | Infantile SMA Onset CS3B Previous ISIS 396443 |

Arm description:

Participants who received nusinersen in study ISIS 396443-CS3B, in the double-blind period, received 3 sham procedures on Days 1, 15, and 64 and 1 loading dose of nusinersen IT injection on Day 29 followed by maintenance doses of nusinersen IT injection, on days 1, 120, 240, 360, 480, 600, 720,

840, 960, 1080, 1200, 1320, 1440, 1560, and 1680 in MMDR period of this study.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Nusinersen |
| Investigational medicinal product code | |
| Other name | ISIS 396443 |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intrathecal use |

Dosage and administration details:

Administered as specified in the treatment arm.

| | |
|---|---|
| **Arm title** | Infantile SMA Onset 232SM202 |

Arm description:

Participants who received nusinersen in study 232SM202 (i.e., Part 2) in an open-label period, received maintenance doses of nusinersen IT injection, on days 1, 120, 240, 360, 480, 600, 720, 840, 960, 1080, 1200, 1320, 1440, 1560, and 1680 in MMDR period of this study.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Nusinersen |
| Investigational medicinal product code | |
| Other name | ISIS 396443 |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intrathecal use |

Dosage and administration details:

Administered as specified in the treatment arm.

| | |
|---|---|
| **Arm title** | Later SMA Onset CS12 Type 2 |

Arm description:

Participants who received nusinersen in study ISIS 396443-CS12 in an open-label period, received maintenance doses of nusinersen IT injection, on days 1, 120, 240, 360, 480, 600, 720, 840, 960, 1080, 1200, 1320, 1440, 1560, and 1680 in MMDR period of this study.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Nusinersen |
| Investigational medicinal product code | |
| Other name | ISIS 396443 |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intrathecal use |

Dosage and administration details:

Administered as specified in the treatment arm.

| | |
|---|---|
| **Arm title** | Later SMA Onset CS12 Type 3 |

Arm description:

Participants who received nusinersen in study ISIS 396443-CS12 in an open-label period, received maintenance doses of nusinersen IT injection, on days 1, 120, 240, 360, 480, 600, 720, 840, 960, 1080, 1200, 1320, 1440, 1560, and 1680 in MMDR period of this study.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Nusinersen |
| Investigational medicinal product code | |
| Other name | ISIS 396443 |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intrathecal use |

Dosage and administration details:

Administered as specified in the treatment arm.

| | |
|---|---|
| **Arm title** | Later SMA Onset CS4 Previous Control |

Arm description:

Participants who received sham procedures in the study ISIS 396443-CS4 in a double-blind period received 3 loading doses of nusinersen administered by IT injection on Days 1, 29, and 85 followed by maintenance doses of nusinersen IT injection, on days 1, 120, 240, 360, 480, 600, 720, 840, 960,

1080, 1200, 1320, 1440, 1560, and 1680 in MMDR period of this study.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Nusinersen |
| Investigational medicinal product code | |
| Other name | ISIS 396443 |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intrathecal use |

Dosage and administration details:

Administered as specified in the treatment arm.

| | |
|---|---|
| **Arm title** | Later SMA Onset CS4 Previous ISIS 396443 |

Arm description:

Participants who received nusinersen in the study ISIS 396443-CS4 in a double-blind period received 2 loading doses of nusinersen administered by IT injection on Days 1 and 85 and 1 sham procedure on Day 29 followed by maintenance doses of nusinersen IT injection, on days 1, 120, 240, 360, 480, 600, 720, 840, 960, 1080, 1200, 1320, 1440, 1560, and 1680 in MMDR period of this study.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Nusinersen |
| Investigational medicinal product code | |
| Other name | ISIS 396443 |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intrathecal use |

Dosage and administration details:

Administered as specified in the treatment arm.

| | |
|---|---|
| **Arm title** | Later SMA Onset 232SM202 |

Arm description:

Participants who received nusinersen in study 232SM202 (i.e., Part 2) in an open-label period, received maintenance doses of nusinersen IT injection, on days 1, 120, 240, 360, 480, 600, 720, 840, 960, 1080, 1200, 1320, 1440, 1560, and 1680 in MMDR period of this study.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Nusinersen |
| Investigational medicinal product code | |
| Other name | ISIS 396443 |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intrathecal use |

Dosage and administration details:

Administered as specified in the treatment arm.

| **Number of subjects in period 1** | Infantile SMA Onset CS3A | Infantile SMA Onset CS3B Previous Control | Infantile SMA Onset CS3B Previous ISIS 396443 |
|---|---|---|---|
| Started | 13 | 24 | 65 |
| Completed | 10 | 10 | 42 |
| Not completed | 3 | 14 | 23 |
| Consent withdrawn by subject | 2 | 3 | 5 |
| Physician decision | - | 2 | - |
| Commercial Drug | - | 1 | 6 |
| Adverse event, non-fatal | - | 5 | 8 |
| Reason Not Specified | 1 | 3 | 4 |

| **Number of subjects in period 1** | Infantile SMA Onset 232SM202 | Later SMA Onset CS12 Type 2 | Later SMA Onset CS12 Type 3 |
|---|---|---|---|
| Started | 12 | 20 | 25 |
| Completed | 7 | 12 | 20 |
| Not completed | 5 | 8 | 5 |
| Consent withdrawn by subject | 1 | 8 | 4 |
| Physician decision | - | - | - |
| Commercial Drug | 3 | - | - |
| Adverse event, non-fatal | 1 | - | - |
| Reason Not Specified | - | - | 1 |

| **Number of subjects in period 1** | Later SMA Onset CS4 Previous Control | Later SMA Onset CS4 Previous ISIS 396443 | Later SMA Onset 232SM202 |
|---|---|---|---|
| Started | 42 | 83 | 8 |
| Completed | 19 | 44 | 5 |
| Not completed | 23 | 39 | 3 |
| Consent withdrawn by subject | 13 | 19 | - |
| Physician decision | - | 1 | - |
| Commercial Drug | 7 | 11 | 2 |
| Adverse event, non-fatal | 2 | 2 | - |
| Reason Not Specified | 1 | 6 | 1 |

## Baseline characteristics

### Reporting groups

| Reporting group title | Infantile SMA Onset CS3A |
|---|---|

Reporting group description:

Participants who received nusinersen in study ISIS 396443-CS3A, in an open-label period, received maintenance doses of nusinersen, intrathecal (IT) injection, on days 1, 120, 240, 360, 480, 600, 720, 840, 960, 1080, 1200, 1320, 1440, 1560, and 1680 in MMDR period of this study.

| Reporting group title | Infantile SMA Onset CS3B Previous Control |
|---|---|

Reporting group description:

Participants who received sham procedures in study ISIS 396443-CS3B, in a double-blind period, received 4 loading doses of nusinersen IT injection on Days 1, 15, 29, and 64 followed by maintenance doses of nusinersen IT injection, on days 1, 120, 240, 360, 480, 600, 720, 840, 960, 1080, 1200, 1320, 1440, 1560, and 1680 in MMDR period of this study.

| Reporting group title | Infantile SMA Onset CS3B Previous ISIS 396443 |
|---|---|

Reporting group description:

Participants who received nusinersen in study ISIS 396443-CS3B, in the double-blind period, received 3 sham procedures on Days 1, 15, and 64 and 1 loading dose of nusinersen IT injection on Day 29 followed by maintenance doses of nusinersen IT injection, on days 1, 120, 240, 360, 480, 600, 720, 840, 960, 1080, 1200, 1320, 1440, 1560, and 1680 in MMDR period of this study.

| Reporting group title | Infantile SMA Onset 232SM202 |
|---|---|

Reporting group description:

Participants who received nusinersen in study 232SM202 (i.e., Part 2) in an open-label period, received maintenance doses of nusinersen IT injection, on days 1, 120, 240, 360, 480, 600, 720, 840, 960, 1080, 1200, 1320, 1440, 1560, and 1680 in MMDR period of this study.

| Reporting group title | Later SMA Onset CS12 Type 2 |
|---|---|

Reporting group description:

Participants who received nusinersen in study ISIS 396443-CS12 in an open-label period, received maintenance doses of nusinersen IT injection, on days 1, 120, 240, 360, 480, 600, 720, 840, 960, 1080, 1200, 1320, 1440, 1560, and 1680 in MMDR period of this study.

| Reporting group title | Later SMA Onset CS12 Type 3 |
|---|---|

Reporting group description:

Participants who received nusinersen in study ISIS 396443-CS12 in an open-label period, received maintenance doses of nusinersen IT injection, on days 1, 120, 240, 360, 480, 600, 720, 840, 960, 1080, 1200, 1320, 1440, 1560, and 1680 in MMDR period of this study.

| Reporting group title | Later SMA Onset CS4 Previous Control |
|---|---|

Reporting group description:

Participants who received sham procedures in the study ISIS 396443-CS4 in a double-blind period received 3 loading doses of nusinersen administered by IT injection on Days 1, 29, and 85 followed by maintenance doses of nusinersen IT injection, on days 1, 120, 240, 360, 480, 600, 720, 840, 960, 1080, 1200, 1320, 1440, 1560, and 1680 in MMDR period of this study.

| Reporting group title | Later SMA Onset CS4 Previous ISIS 396443 |
|---|---|

Reporting group description:

Participants who received nusinersen in the study ISIS 396443-CS4 in a double-blind period received 2 loading doses of nusinersen administered by IT injection on Days 1 and 85 and 1 sham procedure on Day 29 followed by maintenance doses of nusinersen IT injection, on days 1, 120, 240, 360, 480, 600, 720, 840, 960, 1080, 1200, 1320, 1440, 1560, and 1680 in MMDR period of this study.

| Reporting group title | Later SMA Onset 232SM202 |
|---|---|

Reporting group description:

Participants who received nusinersen in study 232SM202 (i.e., Part 2) in an open-label period, received maintenance doses of nusinersen IT injection, on days 1, 120, 240, 360, 480, 600, 720, 840, 960, 1080, 1200, 1320, 1440, 1560, and 1680 in MMDR period of this study.

| Reporting group values | Infantile SMA Onset CS3A | Infantile SMA Onset CS3B Previous Control | Infantile SMA Onset CS3B Previous ISIS 396443 |
|---|---|---|---|
| Number of subjects | 13 | 24 | 65 |
| Age categorical<br>Units: Subjects | | | |
| Infants and toddlers (28 days - 23 months) | 0 | 24 | 65 |
| Children (2 - 11 years) | 13 | 0 | 0 |
| 12 - 17 years | 0 | 0 | 0 |
| Adults (18 - 64 years) | 0 | 0 | 0 |
| Gender categorical<br>Units: Subjects | | | |
| Male | 7 | 9 | 29 |
| Female | 6 | 15 | 36 |
| Ethnicity<br>Units: Subjects | | | |
| Hispanic or Latino | 1 | 3 | 10 |
| Not Hispanic or Latino | 12 | 18 | 47 |
| Not reported | 0 | 3 | 8 |
| Race<br>Units: Subjects | | | |
| American Indian or Alaska native | 0 | 0 | 1 |
| Asian | 1 | 1 | 2 |
| Black or African American | 0 | 0 | 3 |
| White | 10 | 18 | 47 |
| Multiple | 1 | 2 | 1 |
| Other | 1 | 0 | 3 |
| Not reported | 0 | 3 | 8 |

| Reporting group values | Infantile SMA Onset 232SM202 | Later SMA Onset CS12 Type 2 | Later SMA Onset CS12 Type 3 |
|---|---|---|---|
| Number of subjects | 12 | 20 | 25 |
| Age categorical<br>Units: Subjects | | | |
| Infants and toddlers (28 days - 23 months) | 0 | 0 | 0 |
| Children (2 - 11 years) | 12 | 19 | 10 |
| 12 - 17 years | 0 | 0 | 12 |
| Adults (18 - 64 years) | 0 | 1 | 3 |
| Gender categorical<br>Units: Subjects | | | |
| Male | 6 | 12 | 10 |
| Female | 6 | 8 | 15 |
| Ethnicity<br>Units: Subjects | | | |
| Hispanic or Latino | 2 | 2 | 6 |
| Not Hispanic or Latino | 7 | 18 | 19 |
| Not reported | 3 | 0 | 0 |
| Race<br>Units: Subjects | | | |
| American Indian or Alaska native | 0 | 0 | 0 |
| Asian | 4 | 1 | 1 |

| | | | |
|---|---|---|---|
| Black or African American | 0 | 0 | 1 |
| White | 5 | 18 | 23 |
| Multiple | 0 | 1 | 0 |
| Other | 0 | 0 | 0 |
| Not reported | 3 | 0 | 0 |

| **Reporting group values** | Later SMA Onset CS4 Previous Control | Later SMA Onset CS4 Previous ISIS 396443 | Later SMA Onset 232SM202 |
|---|---|---|---|
| Number of subjects | 42 | 83 | 8 |
| Age categorical<br>Units: Subjects | | | |
| Infants and toddlers (28 days - 23 months) | 0 | 0 | 0 |
| Children (2 - 11 years) | 42 | 83 | 8 |
| 12 - 17 years | 0 | 0 | 0 |
| Adults (18 - 64 years) | 0 | 0 | 0 |
| Gender categorical<br>Units: Subjects | | | |
| Male | 21 | 37 | 5 |
| Female | 21 | 46 | 3 |
| Ethnicity<br>Units: Subjects | | | |
| Hispanic or Latino | 0 | 4 | 1 |
| Not Hispanic or Latino | 37 | 69 | 5 |
| Not reported | 5 | 10 | 2 |
| Race<br>Units: Subjects | | | |
| American Indian or Alaska native | 0 | 0 | 1 |
| Asian | 7 | 16 | 0 |
| Black or African American | 1 | 1 | 0 |
| White | 26 | 53 | 4 |
| Multiple | 3 | 3 | 0 |
| Other | 0 | 0 | 1 |
| Not reported | 5 | 10 | 2 |

| **Reporting group values** | Total | | |
|---|---|---|---|
| Number of subjects | 292 | | |
| Age categorical<br>Units: Subjects | | | |
| Infants and toddlers (28 days - 23 months) | 89 | | |
| Children (2 - 11 years) | 187 | | |
| 12 - 17 years | 12 | | |
| Adults (18 - 64 years) | 4 | | |
| Gender categorical<br>Units: Subjects | | | |
| Male | 136 | | |
| Female | 156 | | |
| Ethnicity<br>Units: Subjects | | | |
| Hispanic or Latino | 29 | | |
| Not Hispanic or Latino | 232 | | |

| | | | |
|---|---|---|---|
| Not reported | 31 | | |
| Race<br>Units: Subjects | | | |
| American Indian or Alaska native | 2 | | |
| Asian | 33 | | |
| Black or African American | 6 | | |
| White | 204 | | |
| Multiple | 11 | | |
| Other | 5 | | |
| Not reported | 31 | | |

## End points

### End points reporting groups

| Reporting group title | Infantile SMA Onset CS3A |
|---|---|

Reporting group description:

Participants who received nusinersen in study ISIS 396443-CS3A, in an open-label period, received maintenance doses of nusinersen, intrathecal (IT) injection, on days 1, 120, 240, 360, 480, 600, 720, 840, 960, 1080, 1200, 1320, 1440, 1560, and 1680 in MMDR period of this study.

| Reporting group title | Infantile SMA Onset CS3B Previous Control |
|---|---|

Reporting group description:

Participants who received sham procedures in study ISIS 396443-CS3B, in a double-blind period, received 4 loading doses of nusinersen IT injection on Days 1, 15, 29, and 64 followed by maintenance doses of nusinersen IT injection, on days 1, 120, 240, 360, 480, 600, 720, 840, 960, 1080, 1200, 1320, 1440, 1560, and 1680 in MMDR period of this study.

| Reporting group title | Infantile SMA Onset CS3B Previous ISIS 396443 |
|---|---|

Reporting group description:

Participants who received nusinersen in study ISIS 396443-CS3B, in the double-blind period, received 3 sham procedures on Days 1, 15, and 64 and 1 loading dose of nusinersen IT injection on Day 29 followed by maintenance doses of nusinersen IT injection, on days 1, 120, 240, 360, 480, 600, 720, 840, 960, 1080, 1200, 1320, 1440, 1560, and 1680 in MMDR period of this study.

| Reporting group title | Infantile SMA Onset 232SM202 |
|---|---|

Reporting group description:

Participants who received nusinersen in study 232SM202 (i.e., Part 2) in an open-label period, received maintenance doses of nusinersen IT injection, on days 1, 120, 240, 360, 480, 600, 720, 840, 960, 1080, 1200, 1320, 1440, 1560, and 1680 in MMDR period of this study.

| Reporting group title | Later SMA Onset CS12 Type 2 |
|---|---|

Reporting group description:

Participants who received nusinersen in study ISIS 396443-CS12 in an open-label period, received maintenance doses of nusinersen IT injection, on days 1, 120, 240, 360, 480, 600, 720, 840, 960, 1080, 1200, 1320, 1440, 1560, and 1680 in MMDR period of this study.

| Reporting group title | Later SMA Onset CS12 Type 3 |
|---|---|

Reporting group description:

Participants who received nusinersen in study ISIS 396443-CS12 in an open-label period, received maintenance doses of nusinersen IT injection, on days 1, 120, 240, 360, 480, 600, 720, 840, 960, 1080, 1200, 1320, 1440, 1560, and 1680 in MMDR period of this study.

| Reporting group title | Later SMA Onset CS4 Previous Control |
|---|---|

Reporting group description:

Participants who received sham procedures in the study ISIS 396443-CS4 in a double-blind period received 3 loading doses of nusinersen administered by IT injection on Days 1, 29, and 85 followed by maintenance doses of nusinersen IT injection, on days 1, 120, 240, 360, 480, 600, 720, 840, 960, 1080, 1200, 1320, 1440, 1560, and 1680 in MMDR period of this study.

| Reporting group title | Later SMA Onset CS4 Previous ISIS 396443 |
|---|---|

Reporting group description:

Participants who received nusinersen in the study ISIS 396443-CS4 in a double-blind period received 2 loading doses of nusinersen administered by IT injection on Days 1 and 85 and 1 sham procedure on Day 29 followed by maintenance doses of nusinersen IT injection, on days 1, 120, 240, 360, 480, 600, 720, 840, 960, 1080, 1200, 1320, 1440, 1560, and 1680 in MMDR period of this study.

| Reporting group title | Later SMA Onset 232SM202 |
|---|---|

Reporting group description:

Participants who received nusinersen in study 232SM202 (i.e., Part 2) in an open-label period, received maintenance doses of nusinersen IT injection, on days 1, 120, 240, 360, 480, 600, 720, 840, 960, 1080, 1200, 1320, 1440, 1560, and 1680 in MMDR period of this study.

## Primary: Number of Participants With Treatment-Emergent Adverse Events (AEs) and Serious Adverse Events (SAEs)

| End point title | Number of Participants With Treatment-Emergent Adverse Events (AEs) and Serious Adverse Events (SAEs)[1] |
|---|---|

End point description:

AE:unfavorable and unintended sign, symptom, or disease temporally associated with study/use of an investigational drug, whether or not it's considered related to investigational drug. SAE:AE that in view of either Investigator/Sponsor, meets any of the following criteria: results in death;is life-threatening:i.e.poses risk of death, hospitalization/it's prolongation;results in a persistent or significant incapacity or substantial disruption of normal life functions;results in congenital anomaly or birth defect in offspring;is an important event in the opinion of Investigator/Sponsor. TEAE:if it was present prior to first dose of nusinersen or first sham procedure in index study and subsequently worsened in severity/was not present prior to first dose of nusinersen or first sham procedure in index study but subsequently appeared. The safety analysis set included all participants who were enrolled and received at least 1 dose of nusinersen or underwent sham procedure during CS11.

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

End point timeframe:

From Day 1 up to the end of the study (up to 2848 days)

Notes:

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

| **End point values** | Infantile SMA Onset CS3A | Infantile SMA Onset CS3B Previous Control | Infantile SMA Onset CS3B Previous ISIS 396443 | Infantile SMA Onset 232SM202 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 13 | 24 | 65 | 12 |
| Units: participants | | | | |
| AEs | 13 | 24 | 65 | 12 |
| SAEs | 11 | 23 | 59 | 9 |

| **End point values** | Later SMA Onset CS12 Type 2 | Later SMA Onset CS12 Type 3 | Later SMA Onset CS4 Previous Control | Later SMA Onset CS4 Previous ISIS 396443 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 20 | 25 | 42 | 83 |
| Units: participants | | | | |
| AEs | 20 | 25 | 42 | 80 |
| SAEs | 12 | 6 | 26 | 47 |

| **End point values** | Later SMA Onset 232SM202 | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 8 | | | |
| Units: participants | | | | |
| AEs | 8 | | | |
| SAEs | 5 | | | |

## Statistical analyses

No statistical analyses for this end point

## Primary: Number of Participants With Vital Sign Abnormalities Reported as AEs

| End point title | Number of Participants With Vital Sign Abnormalities Reported as AEs[2] |
|---|---|

End point description:

The vital sign assessments included blood pressure, temperature, pulse rate, and respiratory rate. Participants with abnormalities in these assessments recorded as AEs were reported. The safety analysis set included all participants who were enrolled and received at least 1 dose of nusinersen or underwent sham procedure during CS11.

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

End point timeframe:

From Day 1 up to the end of the study (up to 2848 days)

Notes:

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

| End point values | Infantile SMA Onset CS3A | Infantile SMA Onset CS3B Previous Control | Infantile SMA Onset CS3B Previous ISIS 396443 | Infantile SMA Onset 232SM202 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 13 | 24 | 65 | 12 |
| Units: participants | | | | |
| Bradycardia | 1 | 0 | 6 | 1 |
| Tachycardia | 2 | 4 | 5 | 1 |
| Pyrexia | 13 | 15 | 50 | 5 |
| Body Temperature Increased | 0 | 1 | 1 | 0 |
| Heart Rate Increased | 3 | 2 | 4 | 3 |
| Oxygen Saturation Decreased | 1 | 9 | 20 | 2 |
| Respiratory Rate Increased | 0 | 0 | 1 | 0 |
| Tachypnoea | 0 | 0 | 1 | 1 |

| End point values | Later SMA Onset CS12 Type 2 | Later SMA Onset CS12 Type 3 | Later SMA Onset CS4 Previous Control | Later SMA Onset CS4 Previous ISIS 396443 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 20 | 25 | 42 | 83 |
| Units: participants | | | | |
| Bradycardia | 0 | 0 | 1 | 0 |
| Tachycardia | 0 | 0 | 1 | 2 |
| Pyrexia | 10 | 3 | 21 | 39 |

| | | | | |
|---|---|---|---|---|
| Body Temperature Increased | 0 | 0 | 1 | 0 |
| Heart Rate Increased | 0 | 0 | 2 | 0 |
| Oxygen Saturation Decreased | 0 | 1 | 2 | 3 |
| Respiratory Rate Increased | 0 | 0 | 0 | 0 |
| Tachypnoea | 0 | 0 | 1 | 0 |

| **End point values** | Later SMA Onset 232SM202 | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 8 | | | |
| Units: participants | | | | |
| Bradycardia | 0 | | | |
| Tachycardia | 0 | | | |
| Pyrexia | 5 | | | |
| Body Temperature Increased | 0 | | | |
| Heart Rate Increased | 0 | | | |
| Oxygen Saturation Decreased | 0 | | | |
| Respiratory Rate Increased | 0 | | | |
| Tachypnoea | 0 | | | |

### Statistical analyses

No statistical analyses for this end point

### Primary: Number of Participants With Weight Abnormalities Reported as AEs

| End point title | Number of Participants With Weight Abnormalities Reported as AEs[3] |
|---|---|

End point description:

Weight decrease was characterized by a decrease of >=7% from baseline and weight increase was characterized by an increase of >=7% from baseline. Participants with these abnormalities recorded as AEs were reported. The safety analysis set included all participants who were enrolled and received at least 1 dose of nusinersen or underwent sham procedure during CS11.

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

End point timeframe:

From Day 1 up to the end of the study (up to 2848 days)

Notes:

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

| **End point values** | Infantile SMA Onset CS3A | Infantile SMA Onset CS3B Previous Control | Infantile SMA Onset CS3B Previous ISIS 396443 | Infantile SMA Onset 232SM202 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 13 | 24 | 65 | 12 |
| Units: participants | | | | |
| Weight Decreased | 0 | 0 | 3 | 1 |
| Weight Increased | 0 | 0 | 0 | 0 |

| End point values | Later SMA Onset CS12 Type 2 | Later SMA Onset CS12 Type 3 | Later SMA Onset CS4 Previous Control | Later SMA Onset CS4 Previous ISIS 396443 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 20 | 25 | 42 | 83 |
| Units: participants | | | | |
| Weight Decreased | 0 | 1 | 1 | 3 |
| Weight Increased | 0 | 0 | 5 | 0 |

| End point values | Later SMA Onset 232SM202 | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 8 | | | |
| Units: participants | | | | |
| Weight Decreased | 0 | | | |
| Weight Increased | 0 | | | |

## Statistical analyses

No statistical analyses for this end point

## Primary: Number of Participants With Neurological Abnormalities Reported as AEs

| End point title | Number of Participants With Neurological Abnormalities Reported as AEs[4] |
|---|---|

End point description:

Participants with abnormalities in neurological examinations recorded as AEs were reported. The safety analysis set included all participants who were enrolled and received at least 1 dose of nusinersen or underwent sham procedure during CS11.

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

End point timeframe:

From Day 1 up to the end of the study (up to 2848 days)

Notes:

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

| End point values | Infantile SMA Onset CS3A | Infantile SMA Onset CS3B Previous Control | Infantile SMA Onset CS3B Previous ISIS 396443 | Infantile SMA Onset 232SM202 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 13 | 24 | 65 | 12 |
| Units: participants | | | | |
| Areflexia | 2 | 0 | 1 | 0 |
| Hyporeflexia | 1 | 0 | 0 | 0 |

| | | | | |
|---|---|---|---|---|
| Nystagmus | 0 | 0 | 4 | 1 |
| Motor Dysfunction | 0 | 0 | 1 | 0 |
| Muscle Contractions Involuntary | 0 | 0 | 0 | 1 |
| Myoclonus | 0 | 0 | 0 | 0 |
| Paraesthesia | 0 | 0 | 0 | 0 |
| Tremor | 1 | 0 | 1 | 0 |

| **End point values** | Later SMA Onset CS12 Type 2 | Later SMA Onset CS12 Type 3 | Later SMA Onset CS4 Previous Control | Later SMA Onset CS4 Previous ISIS 396443 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 20 | 25 | 42 | 83 |
| Units: participants | | | | |
| Areflexia | 1 | 0 | 1 | 1 |
| Hyporeflexia | 0 | 0 | 0 | 0 |
| Nystagmus | 0 | 0 | 0 | 0 |
| Motor Dysfunction | 0 | 0 | 0 | 0 |
| Muscle Contractions Involuntary | 2 | 1 | 1 | 4 |
| Myoclonus | 1 | 0 | 0 | 0 |
| Paraesthesia | 0 | 1 | 0 | 1 |
| Tremor | 1 | 1 | 1 | 3 |

| **End point values** | Later SMA Onset 232SM202 | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 8 | | | |
| Units: participants | | | | |
| Areflexia | 0 | | | |
| Hyporeflexia | 0 | | | |
| Nystagmus | 0 | | | |
| Motor Dysfunction | 0 | | | |
| Muscle Contractions Involuntary | 0 | | | |
| Myoclonus | 0 | | | |
| Paraesthesia | 1 | | | |
| Tremor | 0 | | | |

## Statistical analyses

No statistical analyses for this end point

## Primary: Number of Participants With Laboratory Abnormalities Reported as AEs

| End point title | Number of Participants With Laboratory Abnormalities Reported as AEs[5] |
|---|---|

End point description:

Laboratory investigations included hematology, coagulation, serum chemistry and urinalysis parameters. Participants with abnormalities in these laboratory investigations recorded as AEs were reported. The safety analysis set included all participants who were enrolled and received at least 1 dose of nusinersen or underwent sham procedure during CS11.

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

End point timeframe:

From Day 1 up to the end of the study (up to 2848 days)

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: Only descriptive analysis was planned for this endpoint.

| **End point values** | Infantile SMA Onset CS3A | Infantile SMA Onset CS3B Previous Control | Infantile SMA Onset CS3B Previous ISIS 396443 | Infantile SMA Onset 232SM202 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 13 | 24 | 65 | 12 |
| Units: participants | | | | |
| Anaemia | 1 | 0 | 6 | 1 |
| Leukocytosis | 1 | 0 | 3 | 0 |
| Leukopenia | 0 | 1 | 0 | 0 |
| Lymphopenia | 0 | 0 | 0 | 0 |
| Neutropenia | 0 | 0 | 2 | 0 |
| Neutrophilia | 0 | 0 | 2 | 0 |
| Pancytopenia | 0 | 0 | 0 | 0 |
| Thrombocytopenia | 0 | 0 | 1 | 1 |
| Thrombocytosis | 0 | 0 | 0 | 1 |
| Hypertransaminasaemia | 0 | 0 | 1 | 0 |
| Pyuria | 0 | 0 | 0 | 0 |
| Urinary Tract Infection | 3 | 3 | 11 | 1 |
| Alanine Aminotransferase Increased | 0 | 1 | 3 | 0 |
| Aspartate Aminotransferase Increased | 0 | 1 | 2 | 0 |
| Blood Albumin Decreased | 0 | 0 | 0 | 1 |
| Blood Bicarbonate Decreased | 0 | 0 | 2 | 0 |
| Blood Calcium Decreased | 0 | 0 | 1 | 0 |
| Blood Osmolarity Increased | 0 | 0 | 0 | 0 |
| Blood Potassium Abnormal | 0 | 1 | 0 | 0 |
| Blood Potassium Decreased | 0 | 0 | 0 | 1 |
| Blood Potassium Increased | 0 | 0 | 1 | 0 |
| Crystal Urine Present | 0 | 0 | 0 | 0 |
| Full Blood Count Decreased | 0 | 0 | 1 | 0 |
| Full Blood Count Increased | 0 | 0 | 1 | 0 |
| Gamma-Glutamyltransferase Increased | 0 | 2 | 3 | 0 |
| Haemoglobin Decreased | 0 | 1 | 2 | 1 |
| Hepatic Enzyme Increased | 0 | 0 | 1 | 0 |
| Liver Function Test Increased | 0 | 1 | 1 | 0 |
| Mean Platelet Volume Decreased | 0 | 0 | 0 | 1 |
| Neutrophil Count Decreased | 0 | 0 | 0 | 0 |
| Neutrophil Count Increased | 0 | 0 | 1 | 0 |
| Platelet Count Decreased | 0 | 0 | 2 | 0 |
| Platelet Count Increased | 0 | 0 | 0 | 1 |
| Protein Urine Present | 0 | 1 | 1 | 0 |

| | | | | |
|---|---|---|---|---|
| Red Blood Cell Count Increased | 0 | 0 | 0 | 1 |
| Transaminases Increased | 0 | 0 | 0 | 0 |
| Urine Ketone Body Present | 0 | 0 | 0 | 0 |
| White Blood Cell Count Increased | 0 | 0 | 4 | 0 |
| White Blood Cells Urine | 0 | 0 | 1 | 0 |
| White Blood Cells Urine Positive | 0 | 0 | 0 | 1 |
| Hypercalcaemia | 0 | 0 | 1 | 0 |
| Hyperglycaemia | 0 | 0 | 0 | 0 |
| Hypernatraemia | 0 | 0 | 2 | 0 |
| Hypoalbuminaemia | 0 | 0 | 1 | 0 |
| Hypocalcaemia | 0 | 2 | 0 | 0 |
| Hypochloraemia | 0 | 0 | 1 | 1 |
| Hypoglycaemia | 2 | 0 | 5 | 0 |
| Hypokalaemia | 1 | 3 | 10 | 0 |
| Hyponatraemia | 0 | 0 | 1 | 2 |
| Electrolyte Imbalance | 0 | 0 | 1 | 1 |
| Bilirubinuria | 0 | 0 | 0 | 0 |
| Haematuria | 1 | 1 | 0 | 0 |
| Ketonuria | 0 | 0 | 0 | 0 |
| Leukocyturia | 0 | 1 | 0 | 0 |
| Proteinuria | 0 | 1 | 7 | 1 |
| Bandaemia | 0 | 0 | 1 | 0 |

| **End point values** | Later SMA Onset CS12 Type 2 | Later SMA Onset CS12 Type 3 | Later SMA Onset CS4 Previous Control | Later SMA Onset CS4 Previous ISIS 396443 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 20 | 25 | 42 | 83 |
| Units: participants | | | | |
| Anaemia | 2 | 0 | 1 | 1 |
| Leukocytosis | 0 | 0 | 1 | 2 |
| Leukopenia | 0 | 0 | 0 | 1 |
| Lymphopenia | 0 | 0 | 0 | 1 |
| Neutropenia | 0 | 0 | 0 | 0 |
| Neutrophilia | 0 | 0 | 0 | 2 |
| Pancytopenia | 0 | 0 | 0 | 1 |
| Thrombocytopenia | 0 | 0 | 0 | 0 |
| Thrombocytosis | 0 | 0 | 0 | 0 |
| Hypertransaminasaemia | 0 | 0 | 0 | 1 |
| Pyuria | 0 | 1 | 0 | 0 |
| Urinary Tract Infection | 2 | 1 | 4 | 7 |
| Alanine Aminotransferase Increased | 0 | 0 | 0 | 1 |
| Aspartate Aminotransferase Increased | 0 | 0 | 0 | 0 |
| Blood Albumin Decreased | 0 | 0 | 0 | 0 |
| Blood Bicarbonate Decreased | 0 | 0 | 0 | 0 |
| Blood Calcium Decreased | 0 | 0 | 0 | 0 |
| Blood Osmolarity Increased | 0 | 0 | 1 | 0 |
| Blood Potassium Abnormal | 0 | 0 | 0 | 0 |
| Blood Potassium Decreased | 0 | 0 | 0 | 0 |

| | | | | |
|---|---|---|---|---|
| Blood Potassium Increased | 0 | 0 | 0 | 0 |
| Crystal Urine Present | 0 | 0 | 4 | 6 |
| Full Blood Count Decreased | 0 | 0 | 0 | 0 |
| Full Blood Count Increased | 0 | 0 | 0 | 0 |
| Gamma-Glutamyltransferase Increased | 0 | 0 | 0 | 0 |
| Haemoglobin Decreased | 0 | 0 | 0 | 0 |
| Hepatic Enzyme Increased | 0 | 0 | 2 | 0 |
| Liver Function Test Increased | 0 | 0 | 0 | 0 |
| Mean Platelet Volume Decreased | 0 | 0 | 0 | 0 |
| Neutrophil Count Decreased | 0 | 0 | 1 | 0 |
| Neutrophil Count Increased | 0 | 0 | 0 | 0 |
| Platelet Count Decreased | 0 | 0 | 0 | 0 |
| Platelet Count Increased | 0 | 0 | 0 | 0 |
| Protein Urine Present | 0 | 0 | 1 | 3 |
| Red Blood Cell Count Increased | 0 | 0 | 0 | 0 |
| Transaminases Increased | 0 | 0 | 1 | 0 |
| Urine Ketone Body Present | 0 | 0 | 1 | 0 |
| White Blood Cell Count Increased | 0 | 0 | 0 | 0 |
| White Blood Cells Urine | 0 | 0 | 0 | 0 |
| White Blood Cells Urine Positive | 0 | 0 | 0 | 1 |
| Hypercalcaemia | 0 | 0 | 0 | 0 |
| Hyperglycaemia | 0 | 0 | 0 | 2 |
| Hypernatraemia | 0 | 0 | 1 | 1 |
| Hypoalbuminaemia | 0 | 0 | 0 | 0 |
| Hypocalcaemia | 0 | 0 | 0 | 1 |
| Hypochloraemia | 0 | 0 | 0 | 0 |
| Hypoglycaemia | 0 | 0 | 1 | 2 |
| Hypokalaemia | 0 | 0 | 1 | 2 |
| Hyponatraemia | 0 | 0 | 0 | 1 |
| Electrolyte Imbalance | 0 | 0 | 0 | 1 |
| Bilirubinuria | 0 | 0 | 0 | 1 |
| Haematuria | 0 | 1 | 1 | 2 |
| Ketonuria | 0 | 0 | 0 | 1 |
| Leukocyturia | 0 | 0 | 0 | 2 |
| Proteinuria | 0 | 2 | 2 | 8 |
| Bandaemia | 0 | 0 | 0 | 0 |

| **End point values** | Later SMA Onset 232SM202 | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 8 | | | |
| Units: participants | | | | |
| Anaemia | 1 | | | |
| Leukocytosis | 0 | | | |
| Leukopenia | 0 | | | |
| Lymphopenia | 0 | | | |
| Neutropenia | 0 | | | |
| Neutrophilia | 0 | | | |
| Pancytopenia | 0 | | | |

| | | | | |
|---|---|---|---|---|
| Thrombocytopenia | 0 | | | |
| Thrombocytosis | 0 | | | |
| Hypertransaminasaemia | 0 | | | |
| Pyuria | 0 | | | |
| Urinary Tract Infection | 1 | | | |
| Alanine Aminotransferase Increased | 0 | | | |
| Aspartate Aminotransferase Increased | 0 | | | |
| Blood Albumin Decreased | 0 | | | |
| Blood Bicarbonate Decreased | 0 | | | |
| Blood Calcium Decreased | 0 | | | |
| Blood Osmolarity Increased | 0 | | | |
| Blood Potassium Abnormal | 0 | | | |
| Blood Potassium Decreased | 0 | | | |
| Blood Potassium Increased | 0 | | | |
| Crystal Urine Present | 0 | | | |
| Full Blood Count Decreased | 0 | | | |
| Full Blood Count Increased | 0 | | | |
| Gamma-Glutamyltransferase Increased | 0 | | | |
| Haemoglobin Decreased | 0 | | | |
| Hepatic Enzyme Increased | 0 | | | |
| Liver Function Test Increased | 0 | | | |
| Mean Platelet Volume Decreased | 0 | | | |
| Neutrophil Count Decreased | 0 | | | |
| Neutrophil Count Increased | 0 | | | |
| Platelet Count Decreased | 0 | | | |
| Platelet Count Increased | 0 | | | |
| Protein Urine Present | 0 | | | |
| Red Blood Cell Count Increased | 0 | | | |
| Transaminases Increased | 0 | | | |
| Urine Ketone Body Present | 0 | | | |
| White Blood Cell Count Increased | 0 | | | |
| White Blood Cells Urine | 0 | | | |
| White Blood Cells Urine Positive | 0 | | | |
| Hypercalcaemia | 0 | | | |
| Hyperglycaemia | 0 | | | |
| Hypernatraemia | 0 | | | |
| Hypoalbuminaemia | 0 | | | |
| Hypocalcaemia | 0 | | | |
| Hypochloraemia | 0 | | | |
| Hypoglycaemia | 0 | | | |
| Hypokalaemia | 0 | | | |
| Hyponatraemia | 0 | | | |
| Electrolyte Imbalance | 0 | | | |
| Bilirubinuria | 0 | | | |
| Haematuria | 0 | | | |
| Ketonuria | 0 | | | |
| Leukocyturia | 0 | | | |
| Proteinuria | 0 | | | |
| Bandaemia | 0 | | | |

## Statistical analyses

No statistical analyses for this end point

## Primary: Number of Participants With Coagulation Parameters Reported as AEs

| End point title | Number of Participants With Coagulation Parameters Reported as AEs[6] |
|---|---|

End point description:

Coagulation parameters included activated partial thromboplastin time (aPTT) and international normalized ratio (INR). Participants with abnormalities in these coagulation parameters recorded as AEs were reported. The safety analysis set included all participants who were enrolled and received at least 1 dose of nusinersen or underwent sham procedure during CS11.

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

End point timeframe:

From Day 1 up to the end of the study (up to 2848 days)

Notes:

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

| End point values | Infantile SMA Onset CS3A | Infantile SMA Onset CS3B Previous Control | Infantile SMA Onset CS3B Previous ISIS 396443 | Infantile SMA Onset 232SM202 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 13 | 24 | 65 | 12 |
| Units: participants | | | | |
| Activated Partial Thromboplastin Time Prolonged | 1 | 0 | 1 | 0 |
| International Normalised Ratio Abnormal | 0 | 0 | 1 | 0 |
| International Normalised Ratio Decreased | 0 | 0 | 1 | 0 |
| Coagulopathy | 0 | 0 | 1 | 0 |

| End point values | Later SMA Onset CS12 Type 2 | Later SMA Onset CS12 Type 3 | Later SMA Onset CS4 Previous Control | Later SMA Onset CS4 Previous ISIS 396443 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 20 | 25 | 42 | 83 |
| Units: participants | | | | |
| Activated Partial Thromboplastin Time Prolonged | 0 | 0 | 0 | 2 |
| International Normalised Ratio Abnormal | 0 | 0 | 0 | 0 |

| | | | | |
|---|---|---|---|---|
| International Normalised Ratio Decreased | 0 | 0 | 0 | 0 |
| Coagulopathy | 0 | 0 | 0 | 0 |

| **End point values** | Later SMA Onset 232SM202 | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 8 | | | |
| Units: participants | | | | |
| Activated Partial Thromboplastin Time Prolonged | 0 | | | |
| International Normalised Ratio Abnormal | 0 | | | |
| International Normalised Ratio Decreased | 0 | | | |
| Coagulopathy | 0 | | | |

## Statistical analyses

No statistical analyses for this end point

## Primary: Number of Participants With Clinically Significant Shifts in 12 Lead Electrocardiogram (ECG) Results

| End point title | Number of Participants With Clinically Significant Shifts in 12 Lead Electrocardiogram (ECG) Results[7] |
|---|---|

End point description:

Clinical significance of abnormalities in these parameters was determined based on investigator's discretion. The safety analysis set included all participants who were enrolled and received at least 1 dose of nusinersen or underwent sham procedure during CS11.

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

End point timeframe:

From Day 1 up to the end of the study (up to 2848 days)

Notes:

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

| **End point values** | Infantile SMA Onset CS3A | Infantile SMA Onset CS3B Previous Control | Infantile SMA Onset CS3B Previous ISIS 396443 | Infantile SMA Onset 232SM202 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 13 | 22 | 59 | 12 |
| Units: participants | 2 | 1 | 6 | 1 |

| **End point values** | Later SMA Onset CS12 Type 2 | Later SMA Onset CS12 Type 3 | Later SMA Onset CS4 Previous | Later SMA Onset CS4 Previous ISIS |
|---|---|---|---|---|

| | | | Control | 396443 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 20 | 25 | 42 | 83 |
| Units: participants | 0 | 0 | 1 | 1 |

| **End point values** | Later SMA Onset 232SM202 | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 8 | | | |
| Units: participants | 0 | | | |

## Statistical analyses

No statistical analyses for this end point

## Primary: Number of Participants Taking any Concomitant Medication

| End point title | Number of Participants Taking any Concomitant Medication[8] |
|---|---|

End point description:

A concomitant therapy is any non-protocol-specified drug or substance (including over-the-counter medications, herbal medications, and vitamin supplements) administered between the beginning of screening and the last telephone contact or study visit. The safety analysis set included all participants who were enrolled and received at least 1 dose of nusinersen or underwent sham procedure during CS11.

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

End point timeframe:

From Day 1 up to the end of the study (up to 2848 days)

Notes:

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

| **End point values** | Infantile SMA Onset CS3A | Infantile SMA Onset CS3B Previous Control | Infantile SMA Onset CS3B Previous ISIS 396443 | Infantile SMA Onset 232SM202 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 13 | 24 | 65 | 12 |
| Units: participants | 13 | 24 | 65 | 12 |

| **End point values** | Later SMA Onset CS12 Type 2 | Later SMA Onset CS12 Type 3 | Later SMA Onset CS4 Previous Control | Later SMA Onset CS4 Previous ISIS 396443 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 20 | 25 | 42 | 83 |
| Units: participants | 20 | 25 | 42 | 83 |

| End point values | Later SMA Onset 232SM202 | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 8 | | | |
| Units: participants | 8 | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Mean Number of new Motor Milestones Achieved as Assessed by World Health Organization (WHO) Criteria

| End point title | Mean Number of new Motor Milestones Achieved as Assessed by World Health Organization (WHO) Criteria |
|---|---|

End point description:

The WHO motor milestones are a set of six milestones in motor development, all of which would be expected to be attained by 24 months of age in healthy children. The individual milestones are: sitting without support, standing with assistance, hands and knees crawling, walking with assistance, standing alone and walking alone. Mean of number of new milestones achieved was calculated and reported in this outcome measure. The safety analysis set included all participants who were enrolled and received at least 1 dose of nusinersen or underwent sham procedure during CS11. Here, 'Number of subjects analysed' signifies number of participants with data available for endpoint analysis.

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

End point timeframe:

MMDR Period: At Day 1800

| End point values | Infantile SMA Onset CS3A | Infantile SMA Onset CS3B Previous Control | Infantile SMA Onset CS3B Previous ISIS 396443 | Infantile SMA Onset 232SM202 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 9 | 10 | 43 | 8 |
| Units: motor milestone | | | | |
| arithmetic mean (standard deviation) | 0.4 (± 0.73) | 0.0 (± 0.00) | 0.7 (± 1.15) | 0.0 (± 0.53) |

| End point values | Later SMA Onset CS12 Type 2 | Later SMA Onset CS12 Type 3 | Later SMA Onset CS4 Previous Control | Later SMA Onset CS4 Previous ISIS 396443 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 12 | 18 | 19 | 45 |
| Units: motor milestone | | | | |
| arithmetic mean (standard deviation) | -0.6 (± 0.79) | -0.1 (± 0.73) | -0.1 (± 0.32) | -0.2 (± 0.60) |

| End point values | Later SMA Onset 232SM202 | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 6 | | | |
| Units: motor milestone | | | | |
| arithmetic mean (standard deviation) | -0.2 (± 0.75) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants With <2 Years of Age Who Attained Motor Milestones as Assessed by Section 2 of Hammersmith Infant Neurological Examination (HINE)

| End point title | Percentage of Participants With <2 Years of Age Who Attained Motor Milestones as Assessed by Section 2 of Hammersmith Infant Neurological Examination (HINE)[9] |
|---|---|

End point description:

HINE is evaluated in infants between 2-24 months of age. It's a simple, standardized instrument including 26 items assessing different aspects of neurological examinations, such as cranial nerves, posture, movements, tone, and reflexes. In this study, Module 2 of HINE (HINE-2) was assessed, which evaluates 8 developmental milestones (head control, sitting, voluntary grasp, ability to kick, rolling, crawling, standing, and walking) scored on a 3, 4, or 5-point scale, with 0 indicating inability to perform task and score of 2, 3, or 4 indicating full milestone development. Total score is calculated by summing item scores to give maximum possible score of 26. CS3A and CS3B arm/groups were planned to be analysed in this endpoint. Safety analysis set included all participants who were enrolled and received at least 1 dose of nusinersen/underwent sham procedure during CS11. Here, 'Number of subjects analysed' signifies number of participants with data available for endpoint analysis.

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

End point timeframe:

Last observed visit

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: CS3A and CS3B arms were planned to be analysed for this endpoint.

| End point values | Infantile SMA Onset CS3A | Infantile SMA Onset CS3B Previous Control | Infantile SMA Onset CS3B Previous ISIS 396443 | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 8 | 22 | 62 | |
| Units: percentage of participants | | | | |
| number (not applicable) | | | | |
| Head Control:Unable to Maintain Head Upright | 13 | 86 | 34 | |
| Head Control:Wobbles | 13 | 9 | 18 | |
| Head Control:All the Time Maintained Upright | 75 | 5 | 48 | |
| Sitting:Cannot Sit | 13 | 100 | 39 | |

| | | | | |
|---|---|---|---|---|
| Sitting:Sits With Support at Hips | 13 | 0 | 19 | |
| Sitting:Props | 0 | 0 | 8 | |
| Sitting:Stable Sit | 13 | 0 | 19 | |
| Sitting:Pivots (Rotates) | 63 | 0 | 15 | |
| Voluntary Grasp:No Grasp | 0 | 14 | 6 | |
| Voluntary Grasp:Uses Whole Hand | 0 | 55 | 18 | |
| Voluntary Grasp:Index Finger&Thumb;Immature Grasp | 0 | 14 | 21 | |
| Voluntary Grasp:Pincer Grasp | 100 | 18 | 52 | |
| Ability to Kick:No Kicking | 0 | 68 | 18 | |
| Ability to Kick:Kick Horizontally Legs do Not Lift | 13 | 32 | 29 | |
| Ability to Kick:Upward (Vertically) | 0 | 0 | 10 | |
| Ability to Kick:Touches Leg | 0 | 0 | 11 | |
| Ability to Kick:Touches Toes | 88 | 0 | 32 | |
| Rolling:No Rolling | 25 | 91 | 27 | |
| Rolling:Rolling to Side | 0 | 9 | 37 | |
| Rolling:Prone to Supine | 13 | 0 | 5 | |
| Rolling:Supine to Prone | 63 | 0 | 31 | |
| Crawling:Does not Lift Head | 63 | 100 | 81 | |
| Crawling:On Elbow | 0 | 0 | 13 | |
| Crawling:On Outstretched Hand | 0 | 0 | 2 | |
| Crawling:Crawling Flat on Abdomen | 13 | 0 | 3 | |
| Crawling:Crawling on Hands and Knees | 25 | 0 | 2 | |
| Standing:Does not Support Weight | 38 | 100 | 79 | |
| Standing:Supports Weight | 13 | 0 | 11 | |
| Standing:Stands With Support | 25 | 0 | 10 | |
| Standing:Stands Unaided | 25 | 0 | 0 | |
| Walking:No Walking | 75 | 100 | 95 | |
| Walking:Bouncing | 0 | 0 | 0 | |
| Walking:Cruising (Walks Holding on) | 13 | 0 | 5 | |
| Walking:Walking Independently | 13 | 0 | 0 | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Participants who Died or met Permanent Ventilation

| End point title | Number of Participants who Died or met Permanent Ventilation |
|---|---|

End point description:

Permanent ventilation was defined as tracheostomy or >=16 hours of ventilator support per day continuously for >21 days in the absence of an acute reversible event. The safety analysis set included all participants who were enrolled and received at least 1 dose of nusinersen or underwent sham procedure during CS11.

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

End point timeframe:

MMDR Period: Up to Day 1800

| End point values | Infantile SMA Onset CS3A | Infantile SMA Onset CS3B Previous Control | Infantile SMA Onset CS3B Previous ISIS 396443 | Infantile SMA Onset 232SM202 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 13 | 24 | 65 | 12 |
| Units: participants | 0 | 4 | 4 | 1 |

| End point values | Later SMA Onset CS12 Type 2 | Later SMA Onset CS12 Type 3 | Later SMA Onset CS4 Previous Control | Later SMA Onset CS4 Previous ISIS 396443 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 20 | 25 | 42 | 83 |
| Units: participants | 0 | 0 | 0 | 0 |

| End point values | Later SMA Onset 232SM202 | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 8 | | | |
| Units: participants | 0 | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Participants not Requiring Permanent Ventilation

| End point title | Number of Participants not Requiring Permanent Ventilation |
|---|---|

End point description:

The safety analysis set included all participants who were enrolled and received at least 1 dose of nusinersen or underwent sham procedure during CS11.

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

End point timeframe:

MMDR Period: Up to Day 1800

| End point values | Infantile SMA Onset CS3A | Infantile SMA Onset CS3B Previous Control | Infantile SMA Onset CS3B Previous ISIS 396443 | Infantile SMA Onset 232SM202 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 13 | 24 | 65 | 12 |
| Units: participants | 13 | 20 | 61 | 11 |

| End point values | Later SMA Onset CS12 Type 2 | Later SMA Onset CS12 Type 3 | Later SMA Onset CS4 Previous Control | Later SMA Onset CS4 Previous ISIS 396443 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 20 | 25 | 42 | 83 |
| Units: participants | 20 | 25 | 42 | 83 |

| End point values | Later SMA Onset 232SM202 | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 8 | | | |
| Units: participants | 8 | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP INTEND) Motor Function Scale

| End point title | Change From Baseline in Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP INTEND) Motor Function Scale[10] |
|---|---|

End point description:

The CHOP-INTEND test includes 16 items structured to move from easiest to hardest with the grading including gravity eliminated (lower scores) to antigravity movements (higher scores). All item scores range from 0 (worst) to 4 (best). Total scores range from 0 to 64, with higher scores indicating better movement functioning. The safety analysis set included all participants who were enrolled and received at least 1 dose of nusinersen or underwent sham procedure during CS11. Here, 'Number analysed (n)' signifies number of participants with data available for analysis at a specified timepoint. Only CS3A and CS3B arm groups were planned to be analysed for this end point. '99999' signifies that since only one participant was evaluable at Day 2198, standard deviation (SD) was not estimated.

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

End point timeframe:

Baseline, Day 2198

Notes:

[10] - 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: CS3A and CS3B arms were planned to be analysed for this endpoint.

| End point values | Infantile SMA Onset CS3A | Infantile SMA Onset CS3B Previous Control | Infantile SMA Onset CS3B Previous ISIS 396443 | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 13 | 24 | 65 | |
| Units: score on scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n= 13, 24, 65) | 47.4 (± 13.09) | 17.3 (± 9.71) | 38.8 (± 9.43) | |
| Change at Day 2198 (n=1, 10, 29) | -6.0 (± 99999) | 11.5 (± 12.21) | 4.7 (± 14.18) | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Hammersmith Functional Motor Scale Expanded (HFMSE) Total Score

| End point title | Change From Baseline in Hammersmith Functional Motor Scale Expanded (HFMSE) Total Score |
|---|---|

End point description:

The HFMSE consists of 33 scored activities used to assess motor function in children with SMA. Participants were asked to do a specific activity (such as rolling) and they were then graded on the quality and execution of that movement on a scale of 0=being unable, 1=performed with some compensation, and 2=unaided. The overall score is the sum of the scores for all activities with a maximum achievable score of 66. If 6 or fewer items are missing, then these items were imputed to be 0 when summing all 33 items. Higher scores indicate increased motor function. The safety analysis set included all participants who were enrolled and received at least 1 dose of nusinersen or underwent sham procedure during CS11. Here, 'Subjects analysed' signifies number of participants with data available for endpoint analysis. 'Number analysed (n)' signifies number of participants with data available for analysis at specified timepoint.

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

End point timeframe:

MMDR Period: Baseline, MMDR Day 1800

| End point values | Infantile SMA Onset CS3A | Infantile SMA Onset CS3B Previous Control | Infantile SMA Onset CS3B Previous ISIS 396443 | Infantile SMA Onset 232SM202 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 13 | 17 | 49 | 12 |
| Units: score on scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n= 13, 17, 49, 12, 20, 23, 42, 81, 8) | 14.5 (± 13.75) | 0.0 (± 0.00) | 7.3 (± 6.88) | 6.8 (± 6.06) |
| Change at MMDR Day 1800 (n=10,9,3,8,12,17,19,45,6) | 3.4 (± 5.93) | 0.4 (± 0.88) | 6.0 (± 9.12) | -2.3 (± 3.37) |

| End point values | Later SMA Onset CS12 Type 2 | Later SMA Onset CS12 Type 3 | Later SMA Onset CS4 Previous | Later SMA Onset CS4 Previous ISIS |
|---|---|---|---|---|

| | | | Control | 396443 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 20 | 23 | 42 | 81 |
| Units: score on scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n= 13, 17, 49, 12, 20, 23, 42, 81, 8) | 25.6 (± 14.23) | 53.6 (± 8.24) | 22.1 (± 7.75) | 26.1 (± 10.99) |
| Change at MMDR Day 1800 (n=10,9,3,8,12,17,19,45,6) | -7.0 (± 6.03) | -2.4 (± 3.41) | -4.7 (± 7.20) | -6.2 (± 6.36) |

| **End point values** | Later SMA Onset 232SM202 | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 8 | | | |
| Units: score on scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n= 13, 17, 49, 12, 20, 23, 42, 81, 8) | 24.5 (± 12.64) | | | |
| Change at MMDR Day 1800 (n=10,9,3,8,12,17,19,45,6) | -1.2 (± 9.83) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline in Revised Upper Limb Module (RULM) Total Score

| End point title | Change from Baseline in Revised Upper Limb Module (RULM) Total Score |
|---|---|

End point description:

RULM Test is used in participants with SMA to assess upper limb functional ability items and has total of 20 items with an entry item that serves as functional class identification and does not contribute to total score. Remaining 19 scorable items reflect different functional domains and graded on 3-point system with score of 0 (unable), 1 (able, with modification), and 2 (able, no difficulty). There is only 1 item that is scored as a can/cannot score, with 1 as the highest score. Scorable items are summed for total score (0-37), higher scores indicating increased upper limb function. Positive change from baseline indicates improvement. Safety analysis set included all participants who were enrolled&received at least 1 dose of nusinersen/underwent sham procedure during CS11. 'Subjects analysed' signifies number of participants with data available for endpoint analysis. 'Number analysed (n)' signifies number of participants with data available for analysis at specified timepoint.

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

End point timeframe:

MMDR Period: Baseline, MMDR Day 1800

| End point values | Infantile SMA Onset CS3A | Infantile SMA Onset CS3B Previous Control | Infantile SMA Onset CS3B Previous ISIS 396443 | Infantile SMA Onset 232SM202 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 11 | 6 | 18 | 11 |
| Units: score on scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n=11,6,18,11,20,18,42,80,8) | 11.8 (± 7.24) | 1.7 (± 1.63) | 10.3 (± 6.05) | 7.6 (± 6.23) |
| Change at MMDR Day 1800 (n=9,3,12,6,13,9,20,45,6) | 9.1 (± 4.70) | 0.7 (± 0.58) | 10.0 (± 5.38) | 3.3 (± 5.01) |

| End point values | Later SMA Onset CS12 Type 2 | Later SMA Onset CS12 Type 3 | Later SMA Onset CS4 Previous Control | Later SMA Onset CS4 Previous ISIS 396443 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 20 | 18 | 42 | 80 |
| Units: score on scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n=11,6,18,11,20,18,42,80,8) | 24.1 (± 6.14) | 35.9 (± 1.91) | 21.1 (± 4.26) | 23.9 (± 5.69) |
| Change at MMDR Day 1800 (n=9,3,12,6,13,9,20,45,6) | 0.4 (± 3.23) | 0.9 (± 1.76) | 2.4 (± 3.97) | 1.2 (± 3.72) |

| End point values | Later SMA Onset 232SM202 | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 8 | | | |
| Units: score on scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n=11,6,18,11,20,18,42,80,8) | 21.4 (± 8.60) | | | |
| Change at MMDR Day 1800 (n=9,3,12,6,13,9,20,45,6) | 3.2 (± 2.71) | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Total Distance Walked Over Time as Assessed by 6-Minute Walk Test (6MWT)

| End point title | Change From Baseline in Total Distance Walked Over Time as Assessed by 6-Minute Walk Test (6MWT)[11] |
|---|---|

End point description:

The 6MWT measures the distance an individual can walk over a total of six minutes on a hard, flat surface. The goal is for the individual to walk as far as possible in six minutes. Only CS12 Type 2 and CS12 Type 3 arms/ groups were planned to be analysed for this end point. The safety analysis set included all participants who were enrolled and received at least 1 dose of nusinersen or underwent sham procedure during CS11. Here, 'Subjects analysed' signifies number of participants with data

available for endpoint analysis. 'Number analysed (n)' signifies number of participants with data available for analysis at specified timepoint. 99999' signifies that since only one participant was evaluable at Day 2670, standard deviation (SD) was not estimated.

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

End point timeframe:

Baseline, Day 2670

Notes:

[11] - 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: CS12 Type 2 and CS12 Type 3 arms were planned to be analysed for this endpoint.

| **End point values** | Later SMA Onset CS12 Type 2 | Later SMA Onset CS12 Type 3 | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1 | 13 | | |
| Units: meters | | | | |
| arithmetic mean (standard deviation) | 0 (± 99999) | 253.3 (± 182.74) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Participants who Experienced Contracture Assessment

| End point title | Number of Participants who Experienced Contracture Assessment |
|---|---|

End point description:

Contracture assessment is performed to assess the motor performance in SMA. The number of participants who experienced at least one contracture at any location and severe contractures in any of the five locations (hip flexors, knee flexors, ankle planter flexors, elbow flexors, forearm flexors) are reported in this outcome measure. The safety analysis set included all participants who were enrolled and received at least 1 dose of nusinersen or underwent sham procedure during CS11. Here, 'Number of subjects analysed' signifies number of participants with data available for endpoint analysis.

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

End point timeframe:

MMDR Period: At MMDR Day 1800

| **End point values** | Infantile SMA Onset CS3A | Infantile SMA Onset CS3B Previous Control | Infantile SMA Onset CS3B Previous ISIS 396443 | Infantile SMA Onset 232SM202 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 10 | 10 | 41 | 8 |
| Units: participant | | | | |
| At least one contracture at any location | 9 | 10 | 36 | 8 |
| Severe contractures in any of the five locations | 3 | 3 | 16 | 4 |

| End point values | Later SMA Onset CS12 Type 2 | Later SMA Onset CS12 Type 3 | Later SMA Onset CS4 Previous Control | Later SMA Onset CS4 Previous ISIS 396443 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 13 | 18 | 20 | 45 |
| Units: participant | | | | |
| At least one contracture at any location | 13 | 8 | 19 | 44 |
| Severe contractures in any of the five locations | 6 | 1 | 9 | 16 |

| End point values | Later SMA Onset 232SM202 | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 5 | | | |
| Units: participant | | | | |
| At least one contracture at any location | 5 | | | |
| Severe contractures in any of the five locations | 2 | | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change From Baseline in Compound Muscular Action Potential (CMAP)

| End point title | Change From Baseline in Compound Muscular Action Potential (CMAP) |
|---|---|

End point description:

CMAP is an electrophysiological technique that can be used to determine the approximate number of motor neurons in a muscle or group of muscles. Peroneal amplitude (PA) and ulnar amplitude (UA) data is reported in this end point. Score <0 indicated worse response and >0 indicated better response than the normal matched population. Score change <0 indicated worsening and >0 indicated improvement as compared to baseline. The safety analysis set included all participants who were enrolled and received at least 1 dose of nusinersen or underwent sham procedure during CS11. Here, 'Number of subjects analysed' signifies number of participants with data available for endpoint analysis. 'Number analysed (n)' signifies number of participants with data available for analysis at specified timepoint.

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

End point timeframe:

MMDR Period: Baseline, MMDR Day 1800

| End point values | Infantile SMA Onset CS3A | Infantile SMA Onset CS3B Previous Control | Infantile SMA Onset CS3B Previous ISIS 396443 | Infantile SMA Onset 232SM202 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 13 | 22 | 60 | 8 |
| Units: millivolt (mV) | | | | |
| arithmetic mean (standard deviation) | | | | |
| PA:Baseline (n=13,22,60,8,19,22,31,62,6) | 3.02 (± 2.207) | 0.35 (± 0.517) | 1.91 (± 1.367) | 0.94 (± 0.929) |
| PA:Change at MMDRDay1800 (n=9,5,54,6,7,13,13,28,2) | -0.41 (± 1.290) | 0.10 (± 0.243) | 0.30 (± 1.395) | 0.92 (± 1.901) |
| UA:Baseline (n=13,12,60,8,20,23,33,62,6) | 1.52 (± 1.563) | 0.20 (± 0.205) | 0.85 (± 0.944) | 0.99 (± 0.861) |
| UA:Change at MMDRDay1800 (n=9,5,35,6,7,14,13,28,2) | 0.45 (± 0.837) | 0.20 (± 0.188) | 0.67 (± 1.261) | 0.15 (± 0.436) |

| End point values | Later SMA Onset CS12 Type 2 | Later SMA Onset CS12 Type 3 | Later SMA Onset CS4 Previous Control | Later SMA Onset CS4 Previous ISIS 396443 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 19 | 22 | 31 | 62 |
| Units: millivolt (mV) | | | | |
| arithmetic mean (standard deviation) | | | | |
| PA:Baseline (n=13,22,60,8,19,22,31,62,6) | 1.89 (± 1.369) | 2.71 (± 1.318) | 2.00 (± 2.189) | 1.97 (± 1.586) |
| PA:Change at MMDRDay1800 (n=9,5,54,6,7,13,13,28,2) | -0.59 (± 1.069) | -0.08 (± 1.799) | 0.22 (± 4.832) | -0.28 (± 0.924) |
| UA:Baseline (n=13,12,60,8,20,23,33,62,6) | 2.81 (± 1.723) | 6.76 (± 2.448) | 1.69 (± 1.133) | 2.71 (± 2.161) |
| UA:Change at MMDRDay1800 (n=9,5,35,6,7,14,13,28,2) | 0.04 (± 0.957) | 0.04 (± 1.641) | 0.32 (± 1.127) | 0.52 (± 1.60) |

| End point values | Later SMA Onset 232SM202 | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 6 | | | |
| Units: millivolt (mV) | | | | |
| arithmetic mean (standard deviation) | | | | |
| PA:Baseline (n=13,22,60,8,19,22,31,62,6) | 1.35 (± 0.948) | | | |
| PA:Change at MMDRDay1800 (n=9,5,54,6,7,13,13,28,2) | 0.10 (± 1.414) | | | |
| UA:Baseline (n=13,12,60,8,20,23,33,62,6) | 1.25 (± 0.935) | | | |
| UA:Change at MMDRDay1800 (n=9,5,35,6,7,14,13,28,2) | 2.77 (± 2.729) | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Body Length

| End point title | Change From Baseline in Body Length |
|---|---|

End point description:

Participants were analyzed for change in growth parameter of body length to evaluate clinical efficacy. The body length was calculated using either World Health Organization (WHO) or Centers for Disease Control and Prevention (CDC) scales. The CDC scale allows to calculate the body length up to 20 years, while the WHO scale allows to calculate it only up to 10 years. The safety analysis set included all participants who were enrolled and received at least 1 dose of nusinersen or underwent sham procedure during CS11. Here, 'Number of subjects analysed' signifies number of participants with data available for endpoint analysis.

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

End point timeframe:

MMDR Period: Baseline, Day 1800

| End point values | Infantile SMA Onset CS3A | Infantile SMA Onset CS3B Previous Control | Infantile SMA Onset CS3B Previous ISIS 396443 | Infantile SMA Onset 232SM202 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 4 | 7 | 14 | 6 |
| Units: centimetres | | | | |
| arithmetic mean (standard deviation) | 24.2 (± 2.86) | 19.9 (± 6.99) | 29.4 (± 6.38) | 18.8 (± 10.92) |

| End point values | Later SMA Onset CS12 Type 2 | Later SMA Onset CS12 Type 3 | Later SMA Onset CS4 Previous Control | Later SMA Onset CS4 Previous ISIS 396443 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 4 | 1 | 8 | 23 |
| Units: centimetres | | | | |
| arithmetic mean (standard deviation) | 18.8 (± 8.54) | 23.1 (± 0) | 23.7 (± 7.06) | 24.6 (± 10.60) |

| End point values | Later SMA Onset 232SM202 | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 2 | | | |
| Units: centimetres | | | | |
| arithmetic mean (standard deviation) | -10.3 (± 57.63) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Weight

| End point title | Change From Baseline in Weight |
|---|---|

End point description:

Participants were analyzed for change in growth parameter of weight to evaluate clinical efficacy. The weight was calculated using either WHO or CDC scales. The CDC scale allows to calculate the weight up to 20 years, while the WHO scale allows to calculate it only up to 10 years. The safety analysis set included all participants who were enrolled and received at least 1 dose of nusinersen or underwent sham procedure during CS11. Here, 'Number of subjects analysed' signifies number of participants with data available for endpoint analysis.

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

End point timeframe:

MMDR Period: Baseline, Day 1800

| End point values | Infantile SMA Onset CS3A | Infantile SMA Onset CS3B Previous Control | Infantile SMA Onset CS3B Previous ISIS 396443 | Infantile SMA Onset 232SM202 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 9 | 11 | 43 | 8 |
| Units: kilograms (kg) | | | | |
| arithmetic mean (standard deviation) | 9.8 (± 3.48) | 7.7 (± 4.39) | 9.3 (± 3.25) | 9.5 (± 7.04) |

| End point values | Later SMA Onset CS12 Type 2 | Later SMA Onset CS12 Type 3 | Later SMA Onset CS4 Previous Control | Later SMA Onset CS4 Previous ISIS 396443 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 13 | 20 | 20 | 50 |
| Units: kilograms (kg) | | | | |
| arithmetic mean (standard deviation) | 15.1 (± 5.96) | 13.8 (± 14.88) | 15.4 (± 8.05) | 15.2 (± 7.38) |

| End point values | Later SMA Onset 232SM202 | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 6 | | | |
| Units: kilograms (kg) | | | | |
| arithmetic mean (standard deviation) | 11.7 (± 8.09) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Weight for Age Percentile

| End point title | Change From Baseline in Weight for Age Percentile |
|---|---|

End point description:

Participants who were below the age of 36 months were analyzed for change in growth parameter of weight for age to evaluate clinical efficacy. The weight for age percentile was calculated using either WHO or CDC scales. The CDC scale allows to calculate the weight for age percentile up to 20 years, while the WHO scale allows to calculate it only up to 10 years. The safety analysis set included all participants who were enrolled and received at least 1 dose of nusinersen or underwent sham procedure during CS11. Here, 'Number of subjects analysed' signifies number of participants with data available for endpoint analysis.

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

End point timeframe:

MMDR Period: Baseline, Day 1800

| End point values | Infantile SMA Onset CS3A | Infantile SMA Onset CS3B Previous Control | Infantile SMA Onset CS3B Previous ISIS 396443 | Infantile SMA Onset 232SM202 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 8 | 11 | 43 | 6 |
| Units: Percentile | | | | |
| arithmetic mean (standard deviation) | 5.7 (± 27.30) | -5.3 (± 28.97) | 0.3 (± 28.55) | -0.7 (± 25.32) |

| End point values | Later SMA Onset CS12 Type 2 | Later SMA Onset CS12 Type 3 | Later SMA Onset CS4 Previous Control | Later SMA Onset CS4 Previous ISIS 396443 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 0[12] | 0[13] | 9 | 14 |
| Units: Percentile | | | | |
| arithmetic mean (standard deviation) | () | () | 0.9 (± 17.22) | 20.2 (± 28.15) |

Notes:

[12] - None of the participants were below the age of 36 months.

[13] - None of the participants were below the age of 36 months.

| End point values | Later SMA Onset 232SM202 | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 6 | | | |
| Units: Percentile | | | | |
| arithmetic mean (standard deviation) | 4.0 (± 33.11) | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of CMAP Responders

| End point title | Percentage of CMAP Responders |
|---|---|

End point description:

CMAP is an electrophysiological technique that can be used to determine the approximate number of motor neurons in a muscle or group of muscles. A participant was defined as a responder if they had a peroneal amplitude ≥1 mV at last visit (including the amplitude ≥1 mV at baseline and also demonstrated as such at last visit). The safety analysis set included all participants who were enrolled and received at least 1 dose of nusinersen or underwent sham procedure during CS11. Here, 'Number of subjects analysed' signifies number of participants with data available for endpoint analysis.

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

End point timeframe:

MMDR Period: At Day 1800

| End point values | Infantile SMA Onset CS3A | Infantile SMA Onset CS3B Previous Control | Infantile SMA Onset CS3B Previous ISIS 396443 | Infantile SMA Onset 232SM202 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 13 | 22 | 60 | 12 |
| Units: percentage of responders | | | | |
| number (not applicable) | 85 | 0 | 72 | 33 |

| End point values | Later SMA Onset CS12 Type 2 | Later SMA Onset CS12 Type 3 | Later SMA Onset CS4 Previous Control | Later SMA Onset CS4 Previous ISIS 396443 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 20 | 24 | 42 | 81 |
| Units: percentage of responders | | | | |
| number (not applicable) | 65 | 67 | 60 | 51 |

| End point values | Later SMA Onset 232SM202 | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 8 | | | |
| Units: percentage of responders | | | | |
| number (not applicable) | 25 | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Participants who Achieved Motor Milestones

| End point title | Number of Participants who Achieved Motor Milestones |
|---|---|

End point description:

Motor milestones were measured based on WHO criteria. The WHO motor milestones are a set of six milestones in motor development, all of which would be expected to be attained by 24 months of age in healthy children. The individual milestones are: sitting without support (SWS), standing with assistance (SWA), hands and knees crawling (HKC), and walking alone (WA). The safety analysis set included all participants who were enrolled and received at least 1 dose of nusinersen or underwent sham procedure during CS11. Here, 'Number of subjects analysed' signifies number of participants with data available for endpoint analysis.

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

End point timeframe:

MMDR Period: up to Day 1800

| End point values | Infantile SMA Onset CS3A | Infantile SMA Onset CS3B Previous Control | Infantile SMA Onset CS3B Previous ISIS 396443 | Infantile SMA Onset 232SM202 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 12 | 22 | 60 | 12 |
| Units: participants | | | | |
| SWS:Achieved at Baseline&Maintained to Last Visit | 5 | 0 | 16 | 3 |
| SWS:Inability at Baseline, Achieved at Last visit | 3 | 0 | 11 | 0 |
| HKC:Achieved at Baseline&Maintained to Last Visit | 1 | 0 | 0 | 0 |
| HKC: Inability at Baseline, Achieved at Last Visit | 0 | 0 | 4 | 0 |
| SWA:Achieved at Baseline&Maintained to Last Visit | 1 | 0 | 4 | 0 |
| SWA:Inability at Baseline, Achieved at Last Visit | 0 | 0 | 3 | 0 |
| WA:Achieved at Baseline&Maintained to Last Visit | 1 | 0 | 0 | 0 |
| WA:Inability at Baseline, Achieved at Last Visit | 0 | 0 | 1 | 0 |

| End point values | Later SMA Onset CS12 Type 2 | Later SMA Onset CS12 Type 3 | Later SMA Onset CS4 Previous Control | Later SMA Onset CS4 Previous ISIS 396443 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 20 | 24 | 42 | 81 |
| Units: participants | | | | |
| SWS:Achieved at Baseline&Maintained to Last Visit | 13 | 23 | 27 | 58 |
| SWS:Inability at Baseline, Achieved at Last visit | 0 | 0 | 0 | 0 |
| HKC:Achieved at Baseline&Maintained to Last Visit | 4 | 20 | 3 | 18 |
| HKC: Inability at Baseline, Achieved at Last Visit | 0 | 1 | 1 | 2 |

| | | | | |
|---|---|---|---|---|
| SWA:Achieved at Baseline&Maintained to Last Visit | 1 | 20 | 3 | 3 |
| SWA:Inability at Baseline, Achieved at Last Visit | 0 | 0 | 0 | 0 |
| WA:Achieved at Baseline&Maintained to Last Visit | 1 | 16 | 1 | 2 |
| WA:Inability at Baseline, Achieved at Last Visit | 0 | 0 | 0 | 0 |

| **End point values** | Later SMA Onset 232SM202 | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 8 | | | |
| Units: participants | | | | |
| SWS:Achieved at Baseline&Maintained to Last Visit | 5 | | | |
| SWS:Inability at Baseline, Achieved at Last visit | 0 | | | |
| HKC:Achieved at Baseline&Maintained to Last Visit | 2 | | | |
| HKC: Inability at Baseline, Achieved at Last Visit | 1 | | | |
| SWA:Achieved at Baseline&Maintained to Last Visit | 1 | | | |
| SWA:Inability at Baseline, Achieved at Last Visit | 0 | | | |
| WA:Achieved at Baseline&Maintained to Last Visit | 1 | | | |
| WA:Inability at Baseline, Achieved at Last Visit | 0 | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Participants who Achieved Standing Alone and Walking With Assistance

| End point title | Number of Participants who Achieved Standing Alone and Walking With Assistance |
|---|---|

End point description:

Motor milestones were measured based on WHO criteria. The WHO motor milestones are a set of six milestones in motor development, all of which would be expected to be attained by 24 months of age in healthy children. The individual milestones are: sitting without support, standing with assistance, hands and knees crawling, walking with assistance, standing alone and walking alone. Standing alone and walking with assistance was assessed in this outcome measure. The safety analysis set included all participants who were enrolled and received at least 1 dose of nusinersen or underwent sham procedure during CS11. Here, 'Number of subjects analysed' signifies number of participants with data available for endpoint analysis.

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

End point timeframe:

MMDR Period: up to Day 1800

| End point values | Infantile SMA Onset CS3A | Infantile SMA Onset CS3B Previous Control | Infantile SMA Onset CS3B Previous ISIS 396443 | Infantile SMA Onset 232SM202 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 12 | 22 | 60 | 12 |
| Units: participants | | | | |
| Standing alone | 1 | 0 | 0 | 0 |
| Walking with assistance | 2 | 0 | 3 | 0 |

| End point values | Later SMA Onset CS12 Type 2 | Later SMA Onset CS12 Type 3 | Later SMA Onset CS4 Previous Control | Later SMA Onset CS4 Previous ISIS 396443 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 20 | 24 | 42 | 81 |
| Units: participants | | | | |
| Standing alone | 1 | 21 | 2 | 3 |
| Walking with assistance | 3 | 21 | 3 | 7 |

| End point values | Later SMA Onset 232SM202 | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 8 | | | |
| Units: participants | | | | |
| Standing alone | 3 | | | |
| Walking with assistance | 1 | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Total Number of Hospitalizations due to Serious Respiratory Events

| End point title | Total Number of Hospitalizations due to Serious Respiratory Events |
|---|---|

End point description:

Total number of hospitalizations is total number of serious events that occurred during study for all participants under each group. For a participant with multiple SAEs which started at the same date and led to hospitalization, it is counted as one hospitalization. The safety analysis set included all participants who were enrolled and received at least 1 dose of nusinersen or underwent sham procedure during CS11. Here, 'Number of subjects analysed' signifies number of participants with data available for endpoint analysis. 'Number analysed (n)' signifies number of participants with data available for analysis at specified timepoint.

| End point type | Secondary |
|---|---|
| End point timeframe: | |
| Up to day 2520 | |

| **End point values** | Infantile SMA Onset CS3A | Infantile SMA Onset CS3B Previous Control | Infantile SMA Onset CS3B Previous ISIS 396443 | Infantile SMA Onset 232SM202 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 13 | 24 | 64 | 12 |
| Units: number of hospitalizations | | | | |
| number (not applicable) | | | | |
| Day 1-360 (n=13,24,64,12,20,25,42,83,8) | 2 | 12 | 30 | 2 |
| Day 361-720 (n=13,22,61,12,20,25,42,83,8) | 2 | 1 | 18 | 1 |
| Day 721-1080 (n=12,22,60,12,19,24,42,81,8) | 0 | 15 | 12 | 0 |
| Day 1081-1440 (n=12,21,59,11,18,23,39,78,8) | 1 | 0 | 4 | 1 |
| Day 1441-1800 (n=12,18,55,10,18,23,38,76,7) | 2 | 2 | 2 | 2 |
| Day 1801-2160 (n=12,16,52,6,18,23,32,71,1) | 1 | 1 | 7 | 0 |
| Day 2161-2520 (n= 13,10,39,0,12,20,18,48,0) | 0 | 0 | 1 | 0 |

| **End point values** | Later SMA Onset CS12 Type 2 | Later SMA Onset CS12 Type 3 | Later SMA Onset CS4 Previous Control | Later SMA Onset CS4 Previous ISIS 396443 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 20 | 25 | 42 | 83 |
| Units: number of hospitalizations | | | | |
| number (not applicable) | | | | |
| Day 1-360 (n=13,24,64,12,20,25,42,83,8) | 0 | 0 | 2 | 0 |
| Day 361-720 (n=13,22,61,12,20,25,42,83,8) | 1 | 0 | 2 | 1 |
| Day 721-1080 (n=12,22,60,12,19,24,42,81,8) | 0 | 0 | 1 | 2 |
| Day 1081-1440 (n=12,21,59,11,18,23,39,78,8) | 1 | 0 | 1 | 1 |
| Day 1441-1800 (n=12,18,55,10,18,23,38,76,7) | 0 | 0 | 0 | 3 |
| Day 1801-2160 (n=12,16,52,6,18,23,32,71,1) | 0 | 0 | 0 | 1 |
| Day 2161-2520 (n= 13,10,39,0,12,20,18,48,0) | 0 | 0 | 0 | 0 |

| End point values | Later SMA Onset 232SM202 | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 8 | | | |
| Units: number of hospitalizations | | | | |
| number (not applicable) | | | | |
| Day 1-360 (n=13,24,64,12,20,25,42,83,8) | 0 | | | |
| Day 361-720 (n=13,22,61,12,20,25,42,83,8) | 0 | | | |
| Day 721-1080 (n=12,22,60,12,19,24,42,81,8) | 0 | | | |
| Day 1081-1440 (n=12,21,59,11,18,23,39,78,8) | 0 | | | |
| Day 1441-1800 (n=12,18,55,10,18,23,38,76,7) | 0 | | | |
| Day 1801-2160 (n=12,16,52,6,18,23,32,71,1) | 0 | | | |
| Day 2161-2520 (n= 13,10,39,0,12,20,18,48,0) | 0 | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Total Number of Hospitalizations Due to Serious Adverse Events

| End point title | Total Number of Hospitalizations Due to Serious Adverse Events |
|---|---|

End point description:

Total number of hospitalizations is total number of serious events that occurred during study for all participants under each group. For a participant with multiple SAEs which started at the same date and led to hospitalization, it is counted as one hospitalization. The safety analysis set included all participants who were enrolled and received at least 1 dose of nusinersen or underwent sham procedure during CS11. Here, 'Number of subjects analysed' signifies number of participants with data available for endpoint analysis. 'Number analysed (n)' signifies number of participants with data available for analysis at specified timepoint.

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

End point timeframe:

Up to day 2520

| End point values | Infantile SMA Onset CS3A | Infantile SMA Onset CS3B Previous Control | Infantile SMA Onset CS3B Previous ISIS 396443 | Infantile SMA Onset 232SM202 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 13 | 24 | 65 | 12 |
| Units: number of hospitalizations | | | | |
| number (not applicable) | | | | |
| Day 1-360 (n=13,24,65,12,20,25,42,83,8) | 6 | 26 | 89 | 12 |
| Day 361-720 (n=13,22,61,12,20,25,42,83,8) | 6 | 19 | 64 | 4 |

| | | | | |
|---|---|---|---|---|
| Day 721-1080 (n=12,22,60,12,19,24,42,81,8) | 5 | 29 | 63 | 7 |
| Day 1081-1440 (n=12,21,59,11,18,23,39,78,8) | 2 | 10 | 36 | 4 |
| Day 1441-1800 (n=12,18,55,10,18,23,38,76,7) | 4 | 10 | 19 | 3 |
| Day 1801-2160 (n=12,16,52,6,18,23,32,71,1) | 1 | 8 | 32 | 0 |
| Day 2161-2520 (n=13,10,39,0,12,20,18,48,0) | 0 | 1 | 14 | 0 |

| **End point values** | Later SMA Onset CS12 Type 2 | Later SMA Onset CS12 Type 3 | Later SMA Onset CS4 Previous Control | Later SMA Onset CS4 Previous ISIS 396443 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 20 | 25 | 42 | 83 |
| Units: number of hospitalizations | | | | |
| number (not applicable) | | | | |
| Day 1-360 (n=13,24,65,12,20,25,42,83,8) | 2 | 0 | 10 | 8 |
| Day 361-720 (n=13,22,61,12,20,25,42,83,8) | 7 | 2 | 10 | 12 |
| Day 721-1080 (n=12,22,60,12,19,24,42,81,8) | 2 | 0 | 21 | 21 |
| Day 1081-1440 (n=12,21,59,11,18,23,39,78,8) | 5 | 1 | 6 | 10 |
| Day 1441-1800 (n=12,18,55,10,18,23,38,76,7) | 3 | 0 | 5 | 18 |
| Day 1801-2160 (n=12,16,52,6,18,23,32,71,1) | 2 | 2 | 6 | 13 |
| Day 2161-2520 (n=13,10,39,0,12,20,18,48,0) | 0 | 0 | 1 | 2 |

| **End point values** | Later SMA Onset 232SM202 | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 8 | | | |
| Units: number of hospitalizations | | | | |
| number (not applicable) | | | | |
| Day 1-360 (n=13,24,65,12,20,25,42,83,8) | 3 | | | |
| Day 361-720 (n=13,22,61,12,20,25,42,83,8) | 2 | | | |
| Day 721-1080 (n=12,22,60,12,19,24,42,81,8) | 1 | | | |
| Day 1081-1440 (n=12,21,59,11,18,23,39,78,8) | 3 | | | |
| Day 1441-1800 (n=12,18,55,10,18,23,38,76,7) | 0 | | | |
| Day 1801-2160 (n=12,16,52,6,18,23,32,71,1) | 0 | | | |

| | | | | |
|---|---|---|---|---|
| Day 2161-2520 (n=13,10,39,0,12,20,18,48,0) | 0 | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percent of Time in Hospitalization

| End point title | Percent of Time in Hospitalization |
|---|---|

End point description:

The safety analysis set included all participants who were enrolled and received at least 1 dose of nusinersen or underwent sham procedure during CS11. Here, 'Number of subjects analysed' signifies number of participants with data available for endpoint analysis. 'Number analysed (n)' signifies number of participants with data available for analysis at specified timepoint.

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

End point timeframe:

Up to Day 2160

| End point values | Infantile SMA Onset CS3A | Infantile SMA Onset CS3B Previous Control | Infantile SMA Onset CS3B Previous ISIS 396443 | Infantile SMA Onset 232SM202 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 13 | 22 | 60 | 12 |
| Units: percentage of days | | | | |
| median (full range (min-max)) | | | | |
| Day 1-360 (n=13,22,60,12,20,24,42,81,8) | 0.00 (0.00 to 0.2) | 1.11 (0.00 to 16.7) | 0.28 (0.00 to 22.8) | 0.28 (0.00 to 11.4) |
| Day 361-720 (n=12,22,60,12,18,24,42,80,8) | 0.28 (0.00 to 4.7) | 2.08 (0.00 to 17.2) | 0.56 (0.00 to 19.2) | 0.00 (0.00 to 7.8) |
| Day 721-1080 (n=12,20,59,12,18,23,39,78,8) | 0.00 (0.00 to 1.7) | 0.00 (0.00 to 7.5) | 0.00 (0.00 to 31.3) | 0.00 (0.00 to 20.3) |
| Day 1081-1440 (n=12,17,54,11,18,23,36,75,8) | 0.00 (0.00 to 0.8) | 0.00 (0.00 to 7.5) | 0.00 (0.00 to 9.7) | 0.00 (0.00 to 48.6) |
| Day 1441-1800 (n=12,15,50,10,17,23,33,80,7) | 0.00 (0.00 to 8.3) | 0.00 (0.00 to 20.2) | 0.00 (0.00 to 22.6) | 0.00 (0.00 to 12.1) |
| Day 1801-2160 (n=7,8,19,6,10,18,9,31,1) | 0.00 (0.00 to 0.00) | 0.00 (0.00 to 0.00) | 0.00 (0.00 to 0.00) | 0.00 (0.00 to 0.00) |

| End point values | Later SMA Onset CS12 Type 2 | Later SMA Onset CS12 Type 3 | Later SMA Onset CS4 Previous Control | Later SMA Onset CS4 Previous ISIS 396443 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 20 | 24 | 42 | 81 |
| Units: percentage of days | | | | |
| median (full range (min-max)) | | | | |

| | | | | |
|---|---|---|---|---|
| Day 1-360 (n=13,22,60,12,20,24,42,81,8) | 0.00 (0.00 to 2.5) | 0.00 (0.00 to 0.8) | 0.00 (0.00 to 4.4) | 0.00 (0.00 to 6.4) |
| Day 361-720 (n=12,22,60,12,18,24,42,80,8) | 0.00 (0.00 to 3.1) | 0.00 (0.00 to 0.00) | 0.00 (0.00 to 0.00) | 0.00 (0.00 to 29.7) |
| Day 721-1080 (n=12,20,59,12,18,23,39,78,8) | 0.00 (0.00 to 6.1) | 0.00 (0.00 to 1.4) | 0.00 (0.00 to 1.4) | 0.00 (0.00 to 12.2) |
| Day 1081-1440 (n=12,17,54,11,18,23,36,75,8) | 0.00 (0.00 to 1.9) | 0.00 (0.00 to 0.8) | 0.00 (0.00 to 5.8) | 0.00 (0.00 to 35.3) |
| Day 1441-1800 (n=12,15,50,10,17,23,33,80,7) | 0.00 (0.00 to 2.0) | 0.00 (0.00 to 0.8) | 0.00 (0.00 to 5.3) | 0.00 (0.00 to 8.9) |
| Day 1801-2160 (n=7,8,19,6,10,18,9,31,1) | 0.00 (0.00 to 0.00) | 0.00 (0.00 to 0.00) | 0.00 (0.00 to 0.00) | 0.00 (0.00 to 0.00) |

| **End point values** | Later SMA Onset 232SM202 | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 8 | | | |
| Units: percentage of days | | | | |
| median (full range (min-max)) | | | | |
| Day 1-360 (n=13,22,60,12,20,24,42,81,8) | 0.00 (0.00 to 2.8) | | | |
| Day 361-720 (n=12,22,60,12,18,24,42,80,8) | 0.00 (0.00 to 2.5) | | | |
| Day 721-1080 (n=12,20,59,12,18,23,39,78,8) | 0.00 (0.00 to 11.4) | | | |
| Day 1081-1440 (n=12,17,54,11,18,23,36,75,8) | 0.69 (0.00 to 1.9) | | | |
| Day 1441-1800 (n=12,15,50,10,17,23,33,80,7) | 0.00 (0.00 to 1.7) | | | |
| Day 1801-2160 (n=7,8,19,6,10,18,9,31,1) | 0.00 (0.00 to 0.00) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Cobb-Angle on X-Ray of the Thoracolumbar Spine

| End point title | Change From Baseline in Cobb-Angle on X-Ray of the Thoracolumbar Spine |
|---|---|

End point description:

Cobb angle is a measurement of the degree of side-to-side spinal curvature used to define scoliosis. The safety analysis set included all participants who were enrolled and received at least 1 dose of nusinersen or underwent sham procedure during CS11. Here, 'Number of subjects analysed' signifies number of participants with data available for endpoint analysis. 'Number analysed (n)' signifies number of participants with data available for analysis at specified timepoint.

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

End point timeframe:

Baseline, MMDR Day 1800

| End point values | Infantile SMA Onset CS3A | Infantile SMA Onset CS3B Previous Control | Infantile SMA Onset CS3B Previous ISIS 396443 | Infantile SMA Onset 232SM202 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 8 | 11 | 42 | 8 |
| Units: degrees | | | | |
| arithmetic mean (standard deviation) | | | | |
| BL, n= 8,11,42,8,12,10,35,67,5 | 22.7 (± 17.86) | 16.6 (± 13.38) | 34.8 (± 18.43) | 49.2 (± 13.19) |
| Change from BL :MMDRday1800,n=4,4,26,5,4,7,15,30,1 | 29.8 (± 9.46) | 16.9 (± 27.27) | 13.0 (± 29.91) | -11.6 (± 24.65) |

| End point values | Later SMA Onset CS12 Type 2 | Later SMA Onset CS12 Type 3 | Later SMA Onset CS4 Previous Control | Later SMA Onset CS4 Previous ISIS 396443 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 12 | 10 | 35 | 67 |
| Units: degrees | | | | |
| arithmetic mean (standard deviation) | | | | |
| BL, n= 8,11,42,8,12,10,35,67,5 | 38.5 (± 27.36) | 29.8 (± 24.09) | 24.3 (± 19.08) | 26.8 (± 20.33) |
| Change from BL :MMDRday1800,n=4,4,26,5,4,7,15,30,1 | -3.8 (± 17.01) | 4.0 (± 7.78) | 19.8 (± 30.83) | 18.8 (± 30.30) |

| End point values | Later SMA Onset 232SM202 | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 5 | | | |
| Units: degrees | | | | |
| arithmetic mean (standard deviation) | | | | |
| BL, n= 8,11,42,8,12,10,35,67,5 | 33.0 (± 16.94) | | | |
| Change from BL :MMDRday1800,n=4,4,26,5,4,7,15,30,1 | -13.8 (± 0) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Pediatric Quality of Life Inventory (PedsQL) Questionnaires Total Score by Domain

| | |
|---|---|
| End point title | Pediatric Quality of Life Inventory (PedsQL) Questionnaires Total Score by Domain |

End point description:

Items on the PedsQL generic core scale are reverse scored and transformed to a 0-100 scale. The PedsQL parent (P) and self (S) reported questionnaire was collected for participants from 2 to 25 years of age. Four dimensions were collected: Physical, Emotional, Social and School functioning and each item was scored on a 5 point ordinal scale. 0 (never) =100, 1 (almost never) = 75, 2 (sometimes)= 50, 3 (often) = 25, 4 (almost always) = 0. A total score was calculated as the sum of all the items over the number of items answered on all the scales. If more than 50% of items or more were missing, the scale score was not computed. Higher scores indicated better health related quality of life. Safety analysis set. Here, 'Number of subjects analysed' = number of participants with data available for endpoint analysis. 'Number analysed (n)' = number participants with data available for analysis at a specified timepoint.

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

End point timeframe:

MMDR Period: At Day 1800

| **End point values** | Infantile SMA Onset CS3A | Infantile SMA Onset CS3B Previous Control | Infantile SMA Onset CS3B Previous ISIS 396443 | Infantile SMA Onset 232SM202 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 8 | 6 | 28 | 7 |
| Units: score on scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| S:Physical Functioning(n=8,6,28,7,8,11,20,50,5) | 37.1 (± 11.26) | 22.4 (± 31.52) | 47.5 (± 25.31) | 32.6 (± 20.48) |
| S:Emotional Functioning(n=8,6,29,7,8,11,20,50,5) | 61.9 (± 12.52) | 61.7 (± 26.39) | 63.3 (± 20.71) | 67.4 (± 19.55) |
| S:Social Functioning(n=8,6,28,7,8,11,20,50,7) | 67.5 (± 22.83) | 50.8 (± 41.52) | 67.1 (± 22.87) | 75.7 (± 20.09) |
| S:School/Work Functioning(n=8,6,28,5,8,11,20,50,5) | 54.4 (± 14.25) | 40.8 (± 33.23) | 66.1 (± 17.66) | 71.4 (± 14.64) |
| P:Physical Functioning(n=8,10,42,7,8,9,20,49,6) | 25.0 (± 27.55) | 19.1 (± 24.54) | 24.9 (± 22.77) | 32.6 (± 30.07) |
| P:Emotional Functioning(n=8,10,42,7,8,9,20,49,6) | 68.1 (± 13.08) | 69.5 (± 17.23) | 58.7 (± 14.90) | 65.0 (± 26.46) |
| P:Social Functioning(n=8,10,42,7,8,9,20,49,6) | 47.5 (± 12.82) | 50.0 (± 23.66) | 51.3 (± 20.06) | 64.3 (± 22.63) |
| P:School/Work Functioning(n=8,11,42,7,8,9,20,49,5) | 48.8 (± 12.17) | 48.5 (± 31.23) | 51.4 (± 21.36) | 63.6 (± 18.64) |

| **End point values** | Later SMA Onset CS12 Type 2 | Later SMA Onset CS12 Type 3 | Later SMA Onset CS4 Previous Control | Later SMA Onset CS4 Previous ISIS 396443 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 8 | 11 | 20 | 50 |
| Units: score on scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| S:Physical Functioning(n=8,6,28,7,8,11,20,50,5) | 39.8 (± 14.54) | 52.6 (± 21.28) | 45.4 (± 13.85) | 39.7 (± 17.97) |
| S:Emotional Functioning(n=8,6,29,7,8,11,20,50,5) | 76.3 (± 15.29) | 80.0 (± 18.97) | 84.6 (± 15.42) | 74.5 (± 22.80) |
| S:Social Functioning(n=8,6,28,7,8,11,20,50,7) | 76.3 (± 10.94) | 81.4 (± 10.27) | 83.3 (± 15.07) | 76.3 (± 13.88) |

| | | | | |
|---|---|---|---|---|
| S:School/Work Functioning(n=8,6,28,5,8,11,20,50,5) | 75.6 (± 9.43) | 76.4 (± 15.83) | 81.8 (± 14.89) | 77.1 (± 15.22) |
| P:Physical Functioning(n=8,10,42,7,8,9,20,49,6) | 29.3 (± 16.45) | 46.2 (± 76.78) | 35.2 (± 18.19) | 33.5 (± 18.41) |
| P:Emotional Functioning(n=8,10,42,7,8,9,20,49,6) | 70.0 (± 19.46) | 74.4 (± 22.70) | 78.0 (± 18.74) | 78.2 (± 19.60) |
| P:Social Functioning(n=8,10,42,7,8,9,20,49,6) | 64.4 (± 25.70) | 72.2 (± 18.05) | 70.0 (± 20.67) | 71.0 (± 17.50) |
| P:School/Work Functioning(n=8,11,42,7,8,9,20,49,5) | 76.3 (± 10.94) | 77.8 (± 20.78) | 78.8 (± 20.19) | 78.0 (± 14.75) |

| **End point values** | Later SMA Onset 232SM202 | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 5 | | | |
| Units: score on scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| S:Physical Functioning(n=8,6,28,7,8,11,20,50,5) | 53.7 (± 24.46) | | | |
| S:Emotional Functioning(n=8,6,29,7,8,11,20,50,5) | 67.0 (± 16.43) | | | |
| S:Social Functioning(n=8,6,28,7,8,11,20,50,7) | 80.0 (± 12.25) | | | |
| S:School/Work Functioning(n=8,6,28,5,8,11,20,50,5) | 82.0 (± 11.51) | | | |
| P:Physical Functioning(n=8,10,42,7,8,9,20,49,6) | 20.8 (± 5.82) | | | |
| P:Emotional Functioning(n=8,10,42,7,8,9,20,49,6) | 74.2 (± 11.14) | | | |
| P:Social Functioning(n=8,10,42,7,8,9,20,49,6) | 60.8 (± 13.20) | | | |
| P:School/Work Functioning(n=8,11,42,7,8,9,20,49,5) | 79.2 (± 9.70) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Assessment of Caregiver Experience with Neuromuscular Disease (ACEND) Questionnaire Total Score

| End point title | Change From Baseline in Assessment of Caregiver Experience with Neuromuscular Disease (ACEND) Questionnaire Total Score |
|---|---|

End point description:

The ACEND is a questionnaire that includes a total of seven domains assessing physical impact (including feeding/grooming/dressing, sitting/play, transfers, and mobility) and general caregiver impact (including time, emotion, and finance) and each domain comprises several items. The total score (TS) for each domain will be calculated on a scale of 0 to 100. Higher scores indicate a greater impact on the caregiver. The safety analysis set included all participants who were enrolled and received at least 1 dose of nusinersen or underwent sham procedure during CS11. Here, 'Number of subjects analysed' signifies number of participants with data available for endpoint analysis.

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

End point timeframe:
MMDR Period: Baseline, MMDR Day 1800

| **End point values** | Infantile SMA Onset CS3A | Infantile SMA Onset CS3B Previous Control | Infantile SMA Onset CS3B Previous ISIS 396443 | Infantile SMA Onset 232SM202 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 10 | 11 | 38 | 8 |
| Units: score on scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Feeding/Grooming/Dressing TS:Change MMDRDay1800 | 14.2 (± 21.56) | 0.6 (± 2.01) | 18.5 (± 22.07) | 9.2 (± 15.91) |
| Sitting/Play TS: Change at MMDR Day 1800 | 0.8 (± 10.29) | -0.4 (± 14.91) | 5.5 (± 28.01) | 1.5 (± 22.21) |
| Transfers TS: Change at MMDR Day 1800 | 0.4 (± 7.24) | 0.7 (± 1.62) | 0.0 (± 12.32) | -5.5 (± 6.68) |
| Mobility TS: Change at MMDR Day 1800 | -2.3 (± 14.93) | 0.5 (± 1.72) | 7.5 (± 22.52) | -12.1 (± 18.69) |
| Time TS: Change at MMDR Day 1800 | 4.4 (± 19.78) | 6.8 (± 24.76) | -0.7 (± 22.60) | -6.3 (± 21.65) |
| Emotion TS: Change at MMDR Day 1800 | 5.0 (± 14.80) | 6.3 (± 15.82) | -2.1 (± 20.98) | 2.1 (± 14.22) |
| Finance TS: Change at MMDR Day 1800 | -1.0 (± 17.29) | 7.3 (± 20.66) | -4.1 (± 22.17) | 4.4 (± 18.98) |

| **End point values** | Later SMA Onset CS12 Type 2 | Later SMA Onset CS12 Type 3 | Later SMA Onset CS4 Previous Control | Later SMA Onset CS4 Previous ISIS 396443 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 8 | 9 | 18 | 47 |
| Units: score on scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Feeding/Grooming/Dressing TS:Change MMDRDay1800 | 8.3 (± 11.55) | -0.4 (± 1.11) | 4.6 (± 18.90) | 5.9 (± 12.07) |
| Sitting/Play TS: Change at MMDR Day 1800 | 1.0 (± 8.21) | 0.0 (± 0.00) | -1.8 (± 16.48) | 1.7 (± 16.08) |
| Transfers TS: Change at MMDR Day 1800 | -6.4 (± 10.98) | 0.4 (± 3.71) | -3.6 (± 16.17) | 1.2 (± 18.16) |
| Mobility TS: Change at MMDR Day 1800 | -9.6 (± 12.49) | -2.5 (± 6.14) | 1.9 (± 18.47) | -5.8 (± 17.50) |
| Time TS: Change at MMDR Day 1800 | -1.6 (± 21.33) | -2.1 (± 12.10) | 1.4 (± 17.22) | 0.5 (± 16.78) |
| Emotion TS: Change at MMDR Day 1800 | -2.8 (± 26.23) | 1.2 (± 12.96) | 4.7 (± 12.73) | -2.5 (± 12.70) |
| Finance TS: Change at MMDR Day 1800 | 1.9 (± 24.49) | 1.1 (± 8.94) | 7.2 (± 17.92) | 2.1 (± 19.94) |

| **End point values** | Later SMA Onset 232SM202 | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 6 | | | |
| Units: score on scale | | | | |

| | | | | |
|---|---|---|---|---|
| arithmetic mean (standard deviation) | | | | |
| Feeding/Grooming/Dressing TS:Change MMDRDay1800 | 2.8 (± 7.72) | | | |
| Sitting/Play TS: Change at MMDR Day 1800 | -2.0 (± 4.90) | | | |
| Transfers TS: Change at MMDR Day 1800 | -4.0 (± 11.03) | | | |
| Mobility TS: Change at MMDR Day 1800 | 6.7 (± 20.66) | | | |
| Time TS: Change at MMDR Day 1800 | -6.3 (± 14.25) | | | |
| Emotion TS: Change at MMDR Day 1800 | -18.1 (± 12.01) | | | |
| Finance TS: Change at MMDR Day 1800 | -3.3 (± 8.16) | | | |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Number of Participants With Disease-related Hospitalizations and AEs**

| End point title | Number of Participants With Disease-related Hospitalizations and AEs |
|---|---|

End point description:

The safety analysis set included all participants who were enrolled and received at least 1 dose of nusinersen or underwent sham procedure during CS11.

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

End point timeframe:

MMDR Period: up to Day 1800

| **End point values** | Infantile SMA Onset CS3A | Infantile SMA Onset CS3B Previous Control | Infantile SMA Onset CS3B Previous ISIS 396443 | Infantile SMA Onset 232SM202 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 13 | 24 | 65 | 12 |
| Units: participants | | | | |
| Disease-related hospitalization | 6 | 9 | 27 | 5 |
| Disease-related AEs | 11 | 21 | 60 | 7 |

| **End point values** | Later SMA Onset CS12 Type 2 | Later SMA Onset CS12 Type 3 | Later SMA Onset CS4 Previous Control | Later SMA Onset CS4 Previous ISIS 396443 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 20 | 25 | 42 | 83 |
| Units: participants | | | | |
| Disease-related hospitalization | 9 | 0 | 13 | 23 |
| Disease-related AEs | 16 | 12 | 36 | 68 |

| End point values | Later SMA Onset 232SM202 | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 8 | | | |
| Units: participants | | | | |
| Disease-related hospitalization | 1 | | | |
| Disease-related AEs | 8 | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Survival Rate

| End point title | Survival Rate |
|---|---|

End point description:

All dosed population included all participants who received a dose of nusinersen or were in the sham treatment group.

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

End point timeframe:

MMDR Period: up to Day 1800

| End point values | Infantile SMA Onset CS3A | Infantile SMA Onset CS3B Previous Control | Infantile SMA Onset CS3B Previous ISIS 396443 | Infantile SMA Onset 232SM202 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 13 | 24 | 65 | 12 |
| Units: percentage of participants | | | | |
| number (not applicable) | 100 | 79.16 | 87.69 | 91.66 |

| End point values | Later SMA Onset CS12 Type 2 | Later SMA Onset CS12 Type 3 | Later SMA Onset CS4 Previous Control | Later SMA Onset CS4 Previous ISIS 396443 |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 20 | 25 | 42 | 83 |
| Units: percentage of participants | | | | |
| number (not applicable) | 100 | 100 | 97.61 | 98.79 |

| End point values | Later SMA Onset 232SM202 | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 8 | | | |
| Units: percentage of participants | | | | |
| number (not applicable) | 100 | | | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From Day 1 up to the end of the study (up to 2848 days)

Adverse event reporting additional description:

The safety analysis set included all participants who were enrolled and received at least 1 dose of nusinersen or underwent sham procedure during CS11.

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

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 26.0 |

### Reporting groups

| | |
|---|---|
| Reporting group title | Infantile SMA Onset CS3A |

Reporting group description:

Participants who received nusinersen in study ISIS 396443-CS3A, in an open-label period, received maintenance doses of nusinersen, intrathecal (IT) injection, on days 1, 120, 240, 360, 480, 600, 720, 840, 960, 1080, 1200, 1320, 1440, 1560, and 1680 in MMDR period of this study.

| | |
|---|---|
| Reporting group title | Infantile SMA Onset CS3B Previous Control |

Reporting group description:

Participants who received sham procedures in study ISIS 396443-CS3B, in a double-blind period, received 4 loading doses of nusinersen IT injection on Days 1, 15, 29, and 64 followed by maintenance doses of nusinersen IT injection, on days 1, 120, 240, 360, 480, 600, 720, 840, 960, 1080, 1200, 1320, 1440, 1560, and 1680 in MMDR period of this study.

| | |
|---|---|
| Reporting group title | Infantile SMA Onset CS3B Previous ISIS 396443 |

Reporting group description:

Participants who received nusinersen in study ISIS 396443-CS3B, in the double-blind period, received 3 sham procedures on Days 1, 15, and 64 and 1 loading dose of nusinersen IT injection on Day 29 followed by maintenance doses of nusinersen IT injection, on days 1, 120, 240, 360, 480, 600, 720, 840, 960, 1080, 1200, 1320, 1440, 1560, and 1680 in MMDR period of this study.

| | |
|---|---|
| Reporting group title | Infantile SMA Onset 232SM202 |

Reporting group description:

Participants who received nusinersen in study 232SM202 (i.e., Part 2) in an open-label period, received maintenance doses of nusinersen IT injection, on days 1, 120, 240, 360, 480, 600, 720, 840, 960, 1080, 1200, 1320, 1440, 1560, and 1680 in MMDR period of this study.

| | |
|---|---|
| Reporting group title | Later SMA Onset 232SM202 |

Reporting group description:

Participants who received nusinersen in study 232SM202 (i.e., Part 2) in an open-label period, received maintenance doses of nusinersen IT injection, on days 1, 120, 240, 360, 480, 600, 720, 840, 960, 1080, 1200, 1320, 1440, 1560, and 1680 in MMDR period of this study.

| | |
|---|---|
| Reporting group title | Later SMA Onset CS12 Type 3 |

Reporting group description:

Participants who received nusinersen in study ISIS 396443-CS12 in an open-label period, received maintenance doses of nusinersen IT injection, on days 1, 120, 240, 360, 480, 600, 720, 840, 960, 1080, 1200, 1320, 1440, 1560, and 1680 in MMDR period of this study.

| | |
|---|---|
| Reporting group title | Later SMA Onset CS12 Type 2 |

Reporting group description:

Participants who received nusinersen in study ISIS 396443-CS12 in an open-label period, received maintenance doses of nusinersen IT injection, on days 1, 120, 240, 360, 480, 600, 720, 840, 960, 1080, 1200, 1320, 1440, 1560, and 1680 in MMDR period of this study.

| | |
|---|---|
| Reporting group title | Later SMA Onset CS4 Previous Control |

Reporting group description:

Participants who received sham procedures in the study ISIS 396443-CS4 in a double-blind period received 3 loading doses of nusinersen administered by IT injection on Days 1, 29, and 85 followed by maintenance doses of nusinersen IT injection, on days 1, 120, 240, 360, 480, 600, 720, 840, 960, 1080, 1200, 1320, 1440, 1560, and 1680 in MMDR period of this study.

| Reporting group title | Later SMA Onset CS4 Previous ISIS 396443 |
|---|---|

Reporting group description:

Participants who received nusinersen in the study ISIS 396443-CS4 in a double-blind period received 2 loading doses of nusinersen administered by IT injection on Days 1 and 85 and 1 sham procedure on Day 29 followed by maintenance doses of nusinersen IT injection, on days 1, 120, 240, 360, 480, 600, 720, 840, 960, 1080, 1200, 1320, 1440, 1560, and 1680 in MMDR period of this study.

| **Serious adverse events** | Infantile SMA Onset CS3A | Infantile SMA Onset CS3B Previous Control | Infantile SMA Onset CS3B Previous ISIS 396443 |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 11 / 13 (84.62%) | 23 / 24 (95.83%) | 59 / 65 (90.77%) |
| number of deaths (all causes) | 0 | 5 | 8 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Brain stem glioma | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (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 |
| Hair follicle tumour benign | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (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 | | | |
| Hypotension | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 0 / 65 (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 |
| Hypovolaemic shock | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Surgical and medical procedures | | | |
| Positive airway pressure therapy | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| 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 | | | |
|---|---|---|---|
| Death | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Complication of device insertion | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Complication associated with device | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Impaired healing | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (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 |
| Medical device discomfort | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (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 |
| Generalised oedema | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Discomfort | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 24 (4.17%) | 0 / 65 (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 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 2 / 24 (8.33%) | 3 / 65 (4.62%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sudden death | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Immune system disorders | | | |
| Cytokine storm | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anaphylactic reaction | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Reproductive system and breast disorders | | | |
| Testicular torsion | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute respiratory distress syndrome | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (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 |
| Acute respiratory failure | | | |
| subjects affected / exposed | 3 / 13 (23.08%) | 9 / 24 (37.50%) | 15 / 65 (23.08%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 26 | 0 / 29 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Adenoidal hypertrophy | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Apnoea | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 2 / 65 (3.08%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Asthma | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 0 / 65 (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 |
| Aspiration | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Atelectasis | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 5 / 65 (7.69%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchial hyperreactivity | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (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 |
| Chronic respiratory failure | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 2 / 24 (8.33%) | 2 / 65 (3.08%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchial secretion retention | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| 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 / 13 (0.00%) | 1 / 24 (4.17%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Obstructive airways disorder | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypoxia | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 24 (4.17%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Epistaxis | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Obstructive sleep apnoea syndrome | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (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 / 13 (0.00%) | 1 / 24 (4.17%) | 3 / 65 (4.62%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory arrest | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 24 (4.17%) | 2 / 65 (3.08%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Pneumothorax | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 3 / 65 (4.62%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonitis | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 2 / 65 (3.08%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory distress | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 13 (15.38%) | 5 / 24 (20.83%) | 9 / 65 (13.85%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 7 | 0 / 11 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory failure | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 3 / 24 (12.50%) | 9 / 65 (13.85%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 10 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| Respiratory symptom | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sputum increased | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 24 (4.17%) | 0 / 65 (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 |
| Tachypnoea | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (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 |
| Upper respiratory tract inflammation | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Suicidal ideation | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (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 |
| Product issues | | | |
| Device malfunction | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Device mechanical issue | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (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 failure | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 24 (4.17%) | 0 / 65 (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 |
| Investigations | | | |
| Blood culture positive | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Enterovirus test positive | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Coronavirus test positive | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Human rhinovirus test positive | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 24 (4.17%) | 0 / 65 (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 rate increased | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oxygen saturation decreased | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 4 / 24 (16.67%) | 3 / 65 (4.62%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 5 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Respiratory syncytial virus test positive | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rubulavirus test positive | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Accident | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (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 |
| Face injury | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fall | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 2 / 65 (3.08%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Femoral neck fracture | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (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 |
| Femur fracture | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 24 (4.17%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Foreign body aspiration | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrostomy tube site complication | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal stoma complication | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal procedural complication | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Foreign body in respiratory tract | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Joint dislocation | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Limb injury | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (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 procedural complication | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 24 (4.17%) | 0 / 65 (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 |
| Neurological procedural complication | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (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 |
| Post lumbar puncture syndrome | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (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 |
| Post procedural complication | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Post procedural haemorrhage | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Postoperative ileus | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (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 |
| Procedural pain | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (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 |
| Procedural dizziness | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (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 procedural complication | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (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 |
| Unintentional medical device removal | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Wound dehiscence | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Upper limb fracture | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (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 |
| Congenital, familial and genetic disorders | | | |
| Cryptorchism | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Spinal muscular atrophy | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Laryngeal cleft | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Developmental hip dysplasia | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 2 / 65 (3.08%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Talipes | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Cardiac arrest | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 3 / 65 (4.62%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|---|---|---|
| Cardio-respiratory arrest | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 2 / 24 (8.33%) | 3 / 65 (4.62%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 2 |
| Supraventricular extrasystoles | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Wolff-parkinson-white syndrome | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Altered state of consciousness | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Seizure | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 0 / 65 (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 |
| Status epilepticus | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 24 (4.17%) | 0 / 65 (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 |
| Hypoxic-ischaemic encephalopathy | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 24 (4.17%) | 0 / 65 (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 |
| Brain hypoxia | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Syncope | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (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 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Abdominal distension | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| 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 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colitis ulcerative | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (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 |
| Acetonaemic vomiting | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (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 |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 2 / 24 (8.33%) | 0 / 65 (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 |
| Duodenal ulcer haemorrhage | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 24 (4.17%) | 0 / 65 (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 |
| Diarrhoea | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 24 (4.17%) | 0 / 65 (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 |
| Dental caries | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 2 / 65 (3.08%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dysphagia | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 2 / 24 (8.33%) | 0 / 65 (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 |
| Cyclic vomiting syndrome | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (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 |
| Faecaloma | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastritis haemorrhagic | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastritis | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 2 / 65 (3.08%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 3 / 65 (4.62%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gingival hypertrophy | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 0 / 65 (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 |
| Haematemesis | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (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 |
| Hiatus hernia | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (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 |
| Ileus | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancreatitis | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancreatitis acute | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Subileus | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Upper gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 3 / 65 (4.62%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vomiting | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 5 / 65 (7.69%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 6 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| Rash papular | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (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 | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haematuria | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (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 retention | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 24 (4.17%) | 0 / 65 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (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 |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (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 |
| Foot deformity | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (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 |

| | | | |
|---|---|---|---|
| Hip deformity | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pathological fracture | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (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 |
| Neuromuscular scoliosis | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (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 |
| Kyphoscoliosis | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 24 (4.17%) | 4 / 65 (6.15%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Joint contracture | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (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 |
| Retrognathia | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 0 / 65 (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 |
| Scoliosis | | | |
| subjects affected / exposed | 2 / 13 (15.38%) | 0 / 24 (0.00%) | 10 / 65 (15.38%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 11 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Abdominal sepsis | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (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 |
| Acute sinusitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Adenovirus infection | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 3 / 65 (4.62%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (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 |
| Appendicitis perforated | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (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 |
| Bacterial infection | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 2 / 65 (3.08%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cellulitis staphylococcal | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 24 (4.17%) | 0 / 65 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchitis pneumococcal | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 24 (4.17%) | 0 / 65 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 24 (4.17%) | 4 / 65 (6.15%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 6 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchiolitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 24 (4.17%) | 2 / 65 (3.08%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Clostridium difficile infection | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 2 / 65 (3.08%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Coronavirus infection | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 24 (4.17%) | 3 / 65 (4.62%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Coronavirus pneumonia | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Covid-19 | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 3 / 65 (4.62%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Covid-19 pneumonia | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 24 (4.17%) | 2 / 65 (3.08%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Device related infection | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (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 |
| Enterovirus infection | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 24 (4.17%) | 6 / 65 (9.23%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 8 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Escherichia infection | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 4 / 65 (6.15%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastritis viral | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (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 |
| Gastroenteritis adenovirus | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (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 |
| Gastroenteritis viral | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 2 / 65 (3.08%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Human bocavirus infection | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 2 / 65 (3.08%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemophilus infection | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Incision site abscess | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (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 sepsis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (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 / 13 (0.00%) | 0 / 24 (0.00%) | 3 / 65 (4.62%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Laryngitis | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| 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 viral | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| 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 / 13 (0.00%) | 2 / 24 (8.33%) | 7 / 65 (10.77%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 16 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 2 / 65 (3.08%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metapneumovirus infection | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 2 / 24 (8.33%) | 4 / 65 (6.15%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Medical device site abscess | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (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 |
| Osteomyelitis chronic | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Otitis media | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 2 / 65 (3.08%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Otitis media acute | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 24 (4.17%) | 0 / 65 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Otitis media chronic | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Parainfluenzae virus infection | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 24 (4.17%) | 6 / 65 (9.23%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 9 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Periorbital cellulitis | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 24 (4.17%) | 0 / 65 (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 |
| Peritonitis | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (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 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pharyngotonsillitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 0 / 65 (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 |
| Pharyngitis streptococcal | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 24 (4.17%) | 0 / 65 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 3 / 13 (23.08%) | 8 / 24 (33.33%) | 27 / 65 (41.54%) |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 15 | 0 / 44 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Pneumonia aspiration | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 2 / 24 (8.33%) | 6 / 65 (9.23%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 9 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia bacterial | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 4 / 65 (6.15%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia haemophilus | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| 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 influenzal | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 24 (4.17%) | 0 / 65 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia moraxella | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 24 (4.17%) | 0 / 65 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia mycoplasmal | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (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 parainfluenzae viral | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 3 / 65 (4.62%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia serratia | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 3 / 65 (4.62%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia respiratory syncytial viral | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 1 / 24 (4.17%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia pseudomonal | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 2 / 65 (3.08%) |
| 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 viral | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 24 (4.17%) | 3 / 65 (4.62%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Postoperative wound infection | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (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 streptococcal | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (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 |
| Pseudomonas bronchitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| 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 syncytial virus bronchiolitis | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 4 / 65 (6.15%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory syncytial virus infection | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 1 / 24 (4.17%) | 12 / 65 (18.46%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 13 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pseudomonas infection | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 24 (4.17%) | 3 / 65 (4.62%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 6 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulpitis dental | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyuria | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (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 / 13 (0.00%) | 2 / 24 (8.33%) | 8 / 65 (12.31%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 17 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory tract infection viral | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 2 / 24 (8.33%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rhinovirus infection | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 13 (0.00%) | 5 / 24 (20.83%) | 5 / 65 (7.69%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 5 | 0 / 12 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rotavirus infection | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sepsis | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 2 / 65 (3.08%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Staphylococcal bacteraemia | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Staphylococcal infection | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 24 (4.17%) | 2 / 65 (3.08%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Stenotrophomonas infection | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 24 (4.17%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Stoma site infection | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Subcutaneous abscess | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (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 |
| Tracheitis | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 3 / 24 (12.50%) | 5 / 65 (7.69%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 7 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 2 / 65 (3.08%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 24 (4.17%) | 2 / 65 (3.08%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Viral pericarditis | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (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 |
| Varicella | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Viral infection | | | |
| subjects affected / exposed | 2 / 13 (15.38%) | 1 / 24 (4.17%) | 3 / 65 (4.62%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 13 (0.00%) | 2 / 24 (8.33%) | 3 / 65 (4.62%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Failure to thrive | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (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 |
| Feeding intolerance | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 2 / 24 (8.33%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 4 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypoglycaemia | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 4 / 65 (6.15%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypokalaemia | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (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 |
| Malnutrition | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ketoacidosis | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (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 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (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 |
| Metabolic acidosis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 2 / 65 (3.08%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| **Serious adverse events** | Infantile SMA Onset 232SM202 | Later SMA Onset 232SM202 | Later SMA Onset CS12 Type 3 |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 9 / 12 (75.00%) | 5 / 8 (62.50%) | 6 / 25 (24.00%) |
| number of deaths (all causes) | 1 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Brain stem glioma | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Hair follicle tumour benign | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 | | | |
| Hypotension | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Hypovolaemic shock | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Surgical and medical procedures | | | |
| Positive airway pressure therapy | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 | | | |
| Death | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Complication of device insertion | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Complication associated with device | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Impaired healing | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Medical device discomfort | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Generalised oedema | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Discomfort | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Sudden death | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune system disorders | | | |
| Cytokine storm | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Anaphylactic reaction | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Reproductive system and breast disorders | | | |
| Testicular torsion | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 | | | |
| Acute respiratory distress syndrome | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Acute respiratory failure | | | |
| subjects affected / exposed | 2 / 12 (16.67%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Adenoidal hypertrophy | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Apnoea | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Asthma | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Aspiration | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Atelectasis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Bronchial hyperreactivity | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Chronic respiratory failure | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Bronchial secretion retention | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Obstructive airways disorder | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Hypoxia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Epistaxis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Obstructive sleep apnoea syndrome | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 arrest | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 distress | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory failure | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 symptom | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Sputum increased | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Tachypnoea | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Upper respiratory tract inflammation | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Suicidal ideation | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 1 / 25 (4.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Product issues | | | |
| Device malfunction | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 mechanical issue | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 failure | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 | | | |
| Blood culture positive | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Enterovirus test positive | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Coronavirus test positive | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Human rhinovirus test positive | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 rate increased | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Oxygen saturation decreased | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 test positive | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Rubulavirus test positive | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 | | | |
| Accident | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Face injury | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Fall | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 1 / 8 (12.50%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Femoral neck fracture | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Femur fracture | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 1 / 8 (12.50%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Foreign body aspiration | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Gastrostomy tube site complication | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 stoma complication | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 procedural complication | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Foreign body in respiratory tract | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 dislocation | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Limb injury | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 procedural complication | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Neurological procedural complication | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 1 / 25 (4.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Post lumbar puncture syndrome | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 2 / 25 (8.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Post procedural complication | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Post procedural haemorrhage | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Postoperative ileus | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Procedural pain | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Procedural dizziness | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 procedural complication | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Unintentional medical device removal | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Wound dehiscence | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Upper limb fracture | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Congenital, familial and genetic disorders | | | |
| Cryptorchism | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Spinal muscular atrophy | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Laryngeal cleft | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Developmental hip dysplasia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 8 (12.50%) | 0 / 25 (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 |
| Talipes | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Cardiac disorders | | | |
| Cardiac arrest | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |

| | | | |
|---|---|---|---|
| Cardio-respiratory arrest | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Supraventricular extrasystoles | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Wolff-parkinson-white syndrome | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 | | | |
| Altered state of consciousness | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Seizure | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Status epilepticus | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Hypoxic-ischaemic encephalopathy | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Brain hypoxia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Syncope | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 8 (12.50%) | 0 / 25 (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 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 distension | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Colitis ulcerative | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Acetonaemic vomiting | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Duodenal ulcer haemorrhage | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Dental caries | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Cyclic vomiting syndrome | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Faecaloma | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Gastritis haemorrhagic | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Gastritis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 haemorrhage | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Gingival hypertrophy | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Haematemesis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Hiatus hernia | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Ileus | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Pancreatitis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 1 / 25 (4.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancreatitis acute | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Subileus | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Upper gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Skin and subcutaneous tissue disorders | | | |
| Rash papular | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Haematuria | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 1 / 25 (4.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary retention | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Foot deformity | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |

| | | | |
|---|---|---|---|
| Hip deformity | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 8 (12.50%) | 0 / 25 (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 |
| Pathological fracture | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Neuromuscular scoliosis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Kyphoscoliosis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 contracture | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 8 (12.50%) | 0 / 25 (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 |
| Retrognathia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Scoliosis | | | |
| subjects affected / exposed | 3 / 12 (25.00%) | 2 / 8 (25.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Abdominal sepsis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Acute sinusitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Adenovirus infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Appendicitis perforated | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Bacterial infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cellulitis staphylococcal | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 pneumococcal | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Bronchiolitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Clostridium difficile infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Coronavirus infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Coronavirus pneumonia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Covid-19 | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Covid-19 pneumonia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Enterovirus infection | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Escherichia infection | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Gastritis viral | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Gastroenteritis adenovirus | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Gastroenteritis viral | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Human bocavirus infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Haemophilus infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Incision site abscess | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Intestinal sepsis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 viral | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Metapneumovirus infection | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Medical device site abscess | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Osteomyelitis chronic | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 acute | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 chronic | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Parainfluenzae virus infection | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Periorbital cellulitis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Peritonitis | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumococcal bacteraemia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Pharyngotonsillitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Pharyngitis streptococcal | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 | | | |
| subjects affected / exposed | 5 / 12 (41.67%) | 1 / 8 (12.50%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia aspiration | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 bacterial | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Pneumonia haemophilus | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 influenzal | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 moraxella | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 mycoplasmal | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 parainfluenzae viral | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 serratia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 respiratory syncytial viral | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 pseudomonal | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 viral | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Postoperative wound infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 streptococcal | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 8 (12.50%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pseudomonas bronchitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 bronchiolitis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Pseudomonas infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Pulpitis dental | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Pyuria | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 1 / 25 (4.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory tract infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 viral | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Rhinovirus infection | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Rotavirus infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Sepsis | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Staphylococcal bacteraemia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Staphylococcal infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Stenotrophomonas infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Stoma site infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Subcutaneous abscess | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Tracheitis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 pericarditis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Varicella | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 | 2 / 12 (16.67%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Failure to thrive | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Feeding intolerance | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Hypoglycaemia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Hypokalaemia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Malnutrition | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Ketoacidosis | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyponatraemia | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (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 |
| Metabolic acidosis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (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** | Later SMA Onset CS12 Type 2 | Later SMA Onset CS4 Previous Control | Later SMA Onset CS4 Previous ISIS 396443 |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 12 / 20 (60.00%) | 26 / 42 (61.90%) | 47 / 83 (56.63%) |
| number of deaths (all causes) | 0 | 1 | 1 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Brain stem glioma | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 42 (2.38%) | 0 / 83 (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 |
| Hair follicle tumour benign | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 1 / 83 (1.20%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |
| Hypotension | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Hypovolaemic shock | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Surgical and medical procedures | | | |
| Positive airway pressure therapy | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 | | | |
| Death | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Complication of device insertion | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Complication associated with device | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Impaired healing | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 42 (2.38%) | 0 / 83 (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 |
| Medical device discomfort | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Generalised oedema | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Discomfort | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Sudden death | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune system disorders | | | |
| Cytokine storm | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Anaphylactic reaction | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Reproductive system and breast disorders | | | |
| Testicular torsion | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 | | | |
| Acute respiratory distress syndrome | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 1 / 83 (1.20%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Acute respiratory failure | | | |
| subjects affected / exposed | 2 / 20 (10.00%) | 3 / 42 (7.14%) | 1 / 83 (1.20%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 3 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Adenoidal hypertrophy | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Apnoea | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Asthma | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Aspiration | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Atelectasis | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 2 / 83 (2.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchial hyperreactivity | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 42 (2.38%) | 0 / 83 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chronic respiratory failure | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Bronchial secretion retention | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Obstructive airways disorder | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Hypoxia | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Epistaxis | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Obstructive sleep apnoea syndrome | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 1 / 83 (1.20%) |
| 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 arrest | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 distress | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 42 (2.38%) | 1 / 83 (1.20%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory failure | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 42 (2.38%) | 1 / 83 (1.20%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory symptom | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Sputum increased | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Tachypnoea | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 42 (2.38%) | 0 / 83 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Upper respiratory tract inflammation | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Suicidal ideation | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Product issues | | | |
| Device malfunction | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 mechanical issue | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 42 (0.00%) | 0 / 83 (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 failure | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 | | | |
| Blood culture positive | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Enterovirus test positive | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Coronavirus test positive | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Human rhinovirus test positive | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 rate increased | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Oxygen saturation decreased | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 test positive | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Rubulavirus test positive | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 | | | |
| Accident | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 42 (2.38%) | 0 / 83 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Face injury | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Fall | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 42 (2.38%) | 3 / 83 (3.61%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Femoral neck fracture | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 2 / 83 (2.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Femur fracture | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 2 / 42 (4.76%) | 3 / 83 (3.61%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Foreign body aspiration | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Gastrostomy tube site complication | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 stoma complication | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 procedural complication | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Foreign body in respiratory tract | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 dislocation | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 1 / 83 (1.20%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Limb injury | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 1 / 83 (1.20%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal procedural complication | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Neurological procedural complication | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Post lumbar puncture syndrome | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 20 (0.00%) | 2 / 42 (4.76%) | 4 / 83 (4.82%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Post procedural complication | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Post procedural haemorrhage | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Postoperative ileus | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 2 / 83 (2.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Procedural pain | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 1 / 83 (1.20%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Procedural dizziness | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 1 / 83 (1.20%) |
| 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 procedural complication | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Unintentional medical device removal | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Wound dehiscence | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Upper limb fracture | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 1 / 83 (1.20%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Congenital, familial and genetic disorders | | | |
| Cryptorchism | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Spinal muscular atrophy | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Laryngeal cleft | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Developmental hip dysplasia | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 42 (2.38%) | 2 / 83 (2.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Talipes | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Cardiac disorders | | | |
| Cardiac arrest | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |

| | | | |
|---|---|---|---|
| Cardio-respiratory arrest | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Supraventricular extrasystoles | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Wolff-parkinson-white syndrome | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 | | | |
| Altered state of consciousness | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Seizure | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Status epilepticus | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Hypoxic-ischaemic encephalopathy | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Brain hypoxia | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Syncope | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 distension | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 / 20 (0.00%) | 1 / 42 (2.38%) | 0 / 83 (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 |
| Colitis ulcerative | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Acetonaemic vomiting | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 42 (2.38%) | 0 / 83 (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 |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Duodenal ulcer haemorrhage | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Dental caries | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Cyclic vomiting syndrome | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 1 / 83 (1.20%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Faecaloma | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 1 / 83 (1.20%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastritis haemorrhagic | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Gastritis | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 haemorrhage | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Gingival hypertrophy | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Haematemesis | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 1 / 83 (1.20%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hiatus hernia | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Ileus | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Pancreatitis | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 1 / 83 (1.20%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancreatitis acute | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Subileus | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Upper gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Skin and subcutaneous tissue disorders | | | |
| Rash papular | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Haematuria | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 42 (2.38%) | 1 / 83 (1.20%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary retention | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 42 (2.38%) | 0 / 83 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 42 (2.38%) | 0 / 83 (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 |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 42 (2.38%) | 1 / 83 (1.20%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Foot deformity | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 3 / 83 (3.61%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|---|---|---|
| Hip deformity | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Pathological fracture | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Neuromuscular scoliosis | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Kyphoscoliosis | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 42 (2.38%) | 2 / 83 (2.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Joint contracture | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 1 / 83 (1.20%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Retrognathia | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Scoliosis | | | |
| subjects affected / exposed | 6 / 20 (30.00%) | 11 / 42 (26.19%) | 22 / 83 (26.51%) |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 11 | 0 / 22 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Abdominal sepsis | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 1 / 83 (1.20%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Acute sinusitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Adenovirus infection | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 1 / 83 (1.20%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Appendicitis perforated | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 1 / 83 (1.20%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bacterial infection | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cellulitis staphylococcal | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 pneumococcal | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 | 0 / 20 (0.00%) | 1 / 42 (2.38%) | 2 / 83 (2.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchiolitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Clostridium difficile infection | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Coronavirus infection | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 42 (2.38%) | 0 / 83 (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 |
| Coronavirus pneumonia | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Covid-19 | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 1 / 83 (1.20%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Covid-19 pneumonia | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 / 20 (0.00%) | 1 / 42 (2.38%) | 0 / 83 (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 |
| Enterovirus infection | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 3 / 42 (7.14%) | 0 / 83 (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 |
| Escherichia infection | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 2 / 42 (4.76%) | 1 / 83 (1.20%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastritis viral | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Gastroenteritis adenovirus | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 42 (2.38%) | 0 / 83 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis viral | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 2 / 42 (4.76%) | 1 / 83 (1.20%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Human bocavirus infection | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Haemophilus infection | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Incision site abscess | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 sepsis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 1 / 83 (1.20%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Influenza | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 42 (2.38%) | 3 / 83 (3.61%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Laryngitis | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 viral | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 / 20 (0.00%) | 0 / 42 (0.00%) | 1 / 83 (1.20%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Metapneumovirus infection | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 1 / 83 (1.20%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Medical device site abscess | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Osteomyelitis chronic | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 acute | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 chronic | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Parainfluenzae virus infection | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Periorbital cellulitis | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Peritonitis | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Pharyngotonsillitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Pharyngitis streptococcal | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 1 / 83 (1.20%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 2 / 20 (10.00%) | 8 / 42 (19.05%) | 6 / 83 (7.23%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 12 | 0 / 7 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia aspiration | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 42 (2.38%) | 0 / 83 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia bacterial | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 haemophilus | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 influenzal | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 moraxella | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 mycoplasmal | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 1 / 83 (1.20%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia parainfluenzae viral | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 serratia | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 respiratory syncytial viral | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Pneumonia pseudomonal | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 viral | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 1 / 83 (1.20%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Postoperative wound infection | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 1 / 42 (2.38%) | 0 / 83 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia streptococcal | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Pseudomonas bronchitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 bronchiolitis | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 / 20 (0.00%) | 4 / 42 (9.52%) | 3 / 83 (3.61%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 4 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pseudomonas infection | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Pulpitis dental | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Pyuria | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 / 20 (0.00%) | 0 / 42 (0.00%) | 1 / 83 (1.20%) |
| 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 viral | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Rhinovirus infection | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 20 (5.00%) | 2 / 42 (4.76%) | 0 / 83 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rotavirus infection | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Sepsis | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Staphylococcal bacteraemia | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Staphylococcal infection | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Stenotrophomonas infection | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Stoma site infection | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Subcutaneous abscess | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 42 (2.38%) | 0 / 83 (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 |
| Tracheitis | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 42 (2.38%) | 2 / 83 (2.41%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 pericarditis | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 1 / 83 (1.20%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Varicella | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 | 1 / 20 (5.00%) | 0 / 42 (0.00%) | 1 / 83 (1.20%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Failure to thrive | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 42 (2.38%) | 0 / 83 (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 |
| Feeding intolerance | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Hypoglycaemia | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 1 / 83 (1.20%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypokalaemia | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 1 / 83 (1.20%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Malnutrition | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Ketoacidosis | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (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 |
| Metabolic acidosis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 20 (0.00%) | 2 / 42 (4.76%) | 0 / 83 (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 |

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

| **Non-serious adverse events** | Infantile SMA Onset CS3A | Infantile SMA Onset CS3B Previous Control | Infantile SMA Onset CS3B Previous ISIS 396443 |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 13 / 13 (100.00%) | 23 / 24 (95.83%) | 65 / 65 (100.00%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Skin papilloma | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hair follicle tumour benign | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences (all) | 0 | 0 | 1 |
| Hypotension | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 3 / 65 (4.62%) |
| occurrences (all) | 0 | 0 | 3 |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 2 / 24 (8.33%) | 5 / 65 (7.69%) |
| occurrences (all) | 0 | 2 | 5 |
| Developmental delay | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 4 / 65 (6.15%) |
| occurrences (all) | 0 | 0 | 4 |
| Gait disturbance | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infusion site bruising | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Medical device site haemorrhage | | | |
| subjects affected / exposed | 2 / 13 (15.38%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Peripheral swelling | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 2 / 65 (3.08%) |
| occurrences (all) | 1 | 0 | 2 |
| Pneumatosis | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pyrexia | | | |
| subjects affected / exposed | 13 / 13 (100.00%) | 15 / 24 (62.50%) | 50 / 65 (76.92%) |
| occurrences (all) | 66 | 76 | 252 |
| Pain | | | |
| subjects affected / exposed | 2 / 13 (15.38%) | 3 / 24 (12.50%) | 3 / 65 (4.62%) |
| occurrences (all) | 2 | 3 | 3 |
| Immune system disorders | | | |
| Drug hypersensitivity | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 2 / 24 (8.33%) | 1 / 65 (1.54%) |
| occurrences (all) | 0 | 2 | 1 |
| Multiple allergies | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Seasonal allergy | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 3 / 24 (12.50%) | 9 / 65 (13.85%) |
| occurrences (all) | 0 | 5 | 9 |
| Reproductive system and breast disorders | | | |
| Heavy menstrual bleeding | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Testicular atrophy | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute respiratory failure | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 1 / 24 (4.17%) | 4 / 65 (6.15%) |
| occurrences (all) | 1 | 2 | 4 |
| Adenoidal hypertrophy | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 3 / 65 (4.62%) |
| occurrences (all) | 1 | 0 | 5 |
| Aspiration | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 24 (4.17%) | 5 / 65 (7.69%) |
| occurrences (all) | 0 | 1 | 7 |
| Asthma | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Atelectasis | | | |
| subjects affected / exposed | 5 / 13 (38.46%) | 2 / 24 (8.33%) | 9 / 65 (13.85%) |
| occurrences (all) | 6 | 2 | 12 |
| Bronchial wall thickening | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Chronic respiratory failure | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 3 / 24 (12.50%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Epiglottic oedema | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences (all) | 0 | 0 | 1 |
| Emphysema | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Dyspnoea | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 2 / 24 (8.33%) | 3 / 65 (4.62%) |
| occurrences (all) | 1 | 2 | 4 |
| Cough | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 4 / 13 (30.77%) | 4 / 24 (16.67%) | 16 / 65 (24.62%) |
| occurrences (all) | 15 | 5 | 30 |
| Epistaxis | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 1 / 24 (4.17%) | 11 / 65 (16.92%) |
| occurrences (all) | 1 | 1 | 14 |
| Increased upper airway secretion | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 3 / 24 (12.50%) | 6 / 65 (9.23%) |
| occurrences (all) | 0 | 5 | 8 |
| Increased viscosity of upper respiratory secretion | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 2 / 65 (3.08%) |
| occurrences (all) | 1 | 0 | 2 |
| Increased bronchial secretion | | | |
| subjects affected / exposed | 2 / 13 (15.38%) | 4 / 24 (16.67%) | 8 / 65 (12.31%) |
| occurrences (all) | 2 | 4 | 13 |
| Hypoxia | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 1 / 24 (4.17%) | 4 / 65 (6.15%) |
| occurrences (all) | 1 | 1 | 5 |
| Laryngospasm | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lower respiratory tract congestion | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 4 / 65 (6.15%) |
| occurrences (all) | 0 | 0 | 5 |
| Nasal congestion | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 6 / 65 (9.23%) |
| occurrences (all) | 1 | 0 | 11 |
| Lung infiltration | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 1 / 24 (4.17%) | 1 / 65 (1.54%) |
| occurrences (all) | 1 | 1 | 1 |
| Pleural effusion | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 1 / 24 (4.17%) | 0 / 65 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Obstructive sleep apnoea syndrome | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 2 / 65 (3.08%) |
| occurrences (all) | 0 | 0 | 2 |

| | | | |
|---|---|---|---|
| Obstructive airways disorder | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 1 / 24 (4.17%) | 0 / 65 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Noninfective bronchitis | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 24 (4.17%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 1 / 24 (4.17%) | 3 / 65 (4.62%) |
| occurrences (all) | 1 | 1 | 4 |
| Respiratory disorder | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 3 / 65 (4.62%) |
| occurrences (all) | 1 | 0 | 4 |
| Rales | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pulmonary oedema | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Productive cough | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 3 / 65 (4.62%) |
| occurrences (all) | 0 | 0 | 3 |
| Respiratory distress | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 5 / 24 (20.83%) | 5 / 65 (7.69%) |
| occurrences (all) | 1 | 8 | 6 |
| Rhinorrhoea | | | |
| subjects affected / exposed | 2 / 13 (15.38%) | 2 / 24 (8.33%) | 7 / 65 (10.77%) |
| occurrences (all) | 3 | 2 | 10 |
| Rhinitis allergic | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 3 / 24 (12.50%) | 1 / 65 (1.54%) |
| occurrences (all) | 0 | 3 | 1 |
| Restrictive pulmonary disease | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 24 (4.17%) | 1 / 65 (1.54%) |
| occurrences (all) | 0 | 1 | 1 |
| Tonsillar hypertrophy | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 4 / 65 (6.15%) |
| occurrences (all) | 0 | 0 | 6 |

| | | | |
|---|---|---|---|
| Tachypnoea | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences (all) | 0 | 0 | 2 |
| Sputum discoloured | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 1 / 24 (4.17%) | 0 / 65 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Sleep apnoea syndrome | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Wheezing | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 2 / 24 (8.33%) | 1 / 65 (1.54%) |
| occurrences (all) | 0 | 2 | 1 |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 2 / 65 (3.08%) |
| occurrences (all) | 0 | 0 | 2 |
| Agitation | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 1 / 24 (4.17%) | 1 / 65 (1.54%) |
| occurrences (all) | 1 | 1 | 1 |
| Anxiety disorder | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Attention deficit hyperactivity disorder | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 1 / 24 (4.17%) | 1 / 65 (1.54%) |
| occurrences (all) | 1 | 1 | 1 |
| Panic attack | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Mental status changes | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Learning disability | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Irritability | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 13 (0.00%) | 2 / 24 (8.33%) | 4 / 65 (6.15%) |
| occurrences (all) | 0 | 5 | 4 |
| Insomnia | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 2 / 24 (8.33%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Encopresis | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Depression | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Product issues | | | |
| Device malfunction | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences (all) | 0 | 0 | 1 |
| Device dislocation | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 5 / 65 (7.69%) |
| occurrences (all) | 1 | 0 | 10 |
| Investigations | | | |
| Activated partial thromboplastin time prolonged | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences (all) | 1 | 0 | 1 |
| Blood albumin decreased | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood iron decreased | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 3 / 65 (4.62%) |
| occurrences (all) | 0 | 0 | 3 |
| Blood potassium decreased | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Bone density decreased | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 1 / 24 (4.17%) | 1 / 65 (1.54%) |
| occurrences (all) | 1 | 1 | 1 |
| Breath sounds abnormal | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences (all) | 2 | 0 | 1 |
| Cardiac murmur | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Clostridium test positive | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 2 / 24 (8.33%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Heart rate increased | | | |
| subjects affected / exposed | 3 / 13 (23.08%) | 2 / 24 (8.33%) | 4 / 65 (6.15%) |
| occurrences (all) | 4 | 2 | 4 |
| Electrocardiogram qt prolonged | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences (all) | 1 | 0 | 1 |
| Gamma-glutamyltransferase increased | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 2 / 24 (8.33%) | 3 / 65 (4.62%) |
| occurrences (all) | 0 | 2 | 3 |
| Haemoglobin decreased | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 24 (4.17%) | 2 / 65 (3.08%) |
| occurrences (all) | 0 | 1 | 2 |
| Crystal urine present | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oxygen consumption decreased | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Occult blood positive | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences (all) | 0 | 0 | 1 |
| Mean platelet volume decreased | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oxygen saturation decreased | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 7 / 24 (29.17%) | 18 / 65 (27.69%) |
| occurrences (all) | 2 | 9 | 32 |

| | | | |
|---|---|---|---|
| Qrs axis abnormal | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pseudomonas test positive | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 24 (4.17%) | 6 / 65 (9.23%) |
| occurrences (all) | 0 | 1 | 7 |
| Prothrombin time prolonged | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Platelet count increased | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Red blood cell count increased | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Red blood cell sedimentation rate increased | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sars-cov-2 test positive | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences (all) | 1 | 0 | 1 |
| Vitamin d decreased | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| White blood cells urine positive | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Weight increased | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Weight decreased | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 3 / 65 (4.62%) |
| occurrences (all) | 0 | 0 | 3 |
| Von willebrand\'s factor activity decreased | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| White blood cell count increased | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 4 / 65 (6.15%) |
| occurrences (all) | 0 | 0 | 4 |
| Injury, poisoning and procedural complications | | | |
| Contusion | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences (all) | 0 | 0 | 1 |
| Arthropod bite | | | |
| subjects affected / exposed | 2 / 13 (15.38%) | 1 / 24 (4.17%) | 3 / 65 (4.62%) |
| occurrences (all) | 2 | 1 | 3 |
| Concussion | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences (all) | 0 | 0 | 1 |
| Anaesthetic complication neurological | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Anaesthetic complication | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Accident | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences (all) | 1 | 0 | 1 |
| Femur fracture | | | |
| subjects affected / exposed | 2 / 13 (15.38%) | 3 / 24 (12.50%) | 5 / 65 (7.69%) |
| occurrences (all) | 2 | 4 | 7 |
| Fibula fracture | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences (all) | 0 | 0 | 1 |
| Gastrointestinal stoma complication | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Humerus fracture | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 3 / 13 (23.08%) | 1 / 24 (4.17%) | 1 / 65 (1.54%) |
| occurrences (all) | 3 | 1 | 1 |
| Fall | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 3 / 24 (12.50%) | 6 / 65 (9.23%) |
| occurrences (all) | 1 | 3 | 7 |
| Incision site swelling | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Endotracheal intubation complication | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences (all) | 0 | 0 | 1 |
| Extraskeletal ossification | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Immunisation reaction | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences (all) | 0 | 0 | 1 |
| Post procedural contusion | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences (all) | 1 | 0 | 1 |
| Post procedural constipation | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 5 / 65 (7.69%) |
| occurrences (all) | 0 | 0 | 8 |
| Post procedural complication | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 1 / 24 (4.17%) | 1 / 65 (1.54%) |
| occurrences (all) | 1 | 1 | 1 |
| Post lumbar puncture syndrome | | | |
| subjects affected / exposed | 2 / 13 (15.38%) | 4 / 24 (16.67%) | 4 / 65 (6.15%) |
| occurrences (all) | 2 | 4 | 4 |
| Palate injury | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Lower limb fracture | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 24 (4.17%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Post procedural haemorrhage | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 13 (7.69%) | 1 / 24 (4.17%) | 3 / 65 (4.62%) |
| occurrences (all) | 1 | 1 | 3 |
| Ligament sprain | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Joint dislocation | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 1 / 24 (4.17%) | 7 / 65 (10.77%) |
| occurrences (all) | 2 | 1 | 7 |
| Post procedural inflammation | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Procedural hypotension | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Procedural pain | | | |
| subjects affected / exposed | 5 / 13 (38.46%) | 5 / 24 (20.83%) | 15 / 65 (23.08%) |
| occurrences (all) | 6 | 6 | 30 |
| Procedural pneumothorax | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Procedural vomiting | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences (all) | 1 | 0 | 1 |
| Respiratory tract procedural complication | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences (all) | 0 | 0 | 1 |
| Skin abrasion | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 2 / 65 (3.08%) |
| occurrences (all) | 1 | 0 | 2 |
| Stoma site discharge | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences (all) | 0 | 0 | 1 |
| Stoma site erythema | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 24 (4.17%) | 2 / 65 (3.08%) |
| occurrences (all) | 0 | 4 | 2 |

| | | | |
|---|---|---|---|
| Stoma site haemorrhage | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 2 / 24 (8.33%) | 2 / 65 (3.08%) |
| occurrences (all) | 0 | 2 | 2 |
| Stoma site hypergranulation | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 4 / 24 (16.67%) | 5 / 65 (7.69%) |
| occurrences (all) | 0 | 5 | 5 |
| Suture rupture | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tibia fracture | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 2 / 65 (3.08%) |
| occurrences (all) | 1 | 0 | 3 |
| Tooth fracture | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Wound dehiscence | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Wound secretion | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Congenital, familial and genetic disorders | | | |
| Developmental hip dysplasia | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 1 / 24 (4.17%) | 3 / 65 (4.62%) |
| occurrences (all) | 1 | 1 | 3 |
| Cryptorchism | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 1 / 24 (4.17%) | 2 / 65 (3.08%) |
| occurrences (all) | 1 | 1 | 2 |
| High arched palate | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 2 / 24 (8.33%) | 1 / 65 (1.54%) |
| occurrences (all) | 0 | 2 | 1 |
| Cardiac disorders | | | |
| Bradycardia | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 6 / 65 (9.23%) |
| occurrences (all) | 1 | 0 | 7 |
| Tachycardia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 13 (15.38%) | 4 / 24 (16.67%) | 5 / 65 (7.69%) |
| occurrences (all) | 2 | 4 | 7 |
| Sinus tachycardia | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 2 / 24 (8.33%) | 1 / 65 (1.54%) |
| occurrences (all) | 0 | 2 | 1 |
| Right ventricular hypertrophy | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Right atrial enlargement | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences (all) | 1 | 0 | 1 |
| Pericardial effusion | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Nervous system disorders | | | |
| Areflexia | | | |
| subjects affected / exposed | 2 / 13 (15.38%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences (all) | 2 | 0 | 2 |
| Dizziness | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 24 (4.17%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Cognitive disorder | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Disturbance in attention | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Autonomic nervous system imbalance | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 1 / 24 (4.17%) | 0 / 65 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Dysarthria | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences (all) | 1 | 0 | 1 |
| Migraine | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lethargy | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Intracranial pressure increased | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyporeflexia | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Horner\'s syndrome | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Headache | | | |
| subjects affected / exposed | 4 / 13 (30.77%) | 3 / 24 (12.50%) | 8 / 65 (12.31%) |
| occurrences (all) | 4 | 3 | 9 |
| Motor developmental delay | | | |
| subjects affected / exposed | 3 / 13 (23.08%) | 0 / 24 (0.00%) | 2 / 65 (3.08%) |
| occurrences (all) | 3 | 0 | 2 |
| Paraesthesia | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nystagmus | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 4 / 65 (6.15%) |
| occurrences (all) | 0 | 0 | 4 |
| Myoclonus | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Muscle contractions involuntary | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tremor | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences (all) | 1 | 0 | 1 |
| Blood and lymphatic system disorders | | | |

| | | | |
|---|---|---|---|
| Thrombocytosis | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Thrombocytopenia | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences (all) | 0 | 0 | 2 |
| Lymphadenopathy | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Leukocytosis | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 3 / 65 (4.62%) |
| occurrences (all) | 1 | 0 | 3 |
| Iron deficiency anaemia | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 2 / 24 (8.33%) | 2 / 65 (3.08%) |
| occurrences (all) | 0 | 2 | 2 |
| Anaemia | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 6 / 65 (9.23%) |
| occurrences (all) | 1 | 0 | 8 |
| Ear and labyrinth disorders | | | |
| Cerumen impaction | | | |
| subjects affected / exposed | 2 / 13 (15.38%) | 2 / 24 (8.33%) | 0 / 65 (0.00%) |
| occurrences (all) | 2 | 2 | 0 |
| Ear pain | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 2 / 65 (3.08%) |
| occurrences (all) | 1 | 0 | 7 |
| Hyperacusis | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Myringosclerosis | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Motion sickness | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eye disorders | | | |

| | | | |
|---|---|---|---|
| Amblyopia | | | |
| subjects affected / exposed | 2 / 13 (15.38%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences (all) | 2 | 0 | 1 |
| Astigmatism | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 2 / 24 (8.33%) | 3 / 65 (4.62%) |
| occurrences (all) | 1 | 2 | 3 |
| Chalazion | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 2 / 24 (8.33%) | 1 / 65 (1.54%) |
| occurrences (all) | 0 | 3 | 1 |
| Eyelid cyst | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hypermetropia | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences (all) | 1 | 0 | 1 |
| Strabismus | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 24 (4.17%) | 4 / 65 (6.15%) |
| occurrences (all) | 0 | 1 | 5 |
| Myopia | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 1 / 24 (4.17%) | 2 / 65 (3.08%) |
| occurrences (all) | 1 | 1 | 2 |
| Gastrointestinal disorders | | | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 24 (4.17%) | 1 / 65 (1.54%) |
| occurrences (all) | 0 | 1 | 1 |
| Abdominal distension | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 4 / 65 (6.15%) |
| occurrences (all) | 0 | 0 | 6 |
| Abdominal pain | | | |
| subjects affected / exposed | 2 / 13 (15.38%) | 1 / 24 (4.17%) | 4 / 65 (6.15%) |
| occurrences (all) | 3 | 2 | 5 |
| Colitis ulcerative | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Constipation | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 3 / 13 (23.08%) | 7 / 24 (29.17%) | 22 / 65 (33.85%) |
| occurrences (all) | 4 | 14 | 28 |
| Diarrhoea | | | |
| subjects affected / exposed | 4 / 13 (30.77%) | 8 / 24 (33.33%) | 16 / 65 (24.62%) |
| occurrences (all) | 5 | 11 | 18 |
| Dyspepsia | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrointestinal motility disorder | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastritis | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 1 / 24 (4.17%) | 2 / 65 (3.08%) |
| occurrences (all) | 1 | 1 | 3 |
| Gastritis haemorrhagic | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 5 / 24 (20.83%) | 2 / 65 (3.08%) |
| occurrences (all) | 0 | 6 | 4 |
| Dysphagia | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 2 / 24 (8.33%) | 5 / 65 (7.69%) |
| occurrences (all) | 0 | 2 | 5 |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 4 / 24 (16.67%) | 9 / 65 (13.85%) |
| occurrences (all) | 0 | 4 | 10 |
| Hiatus hernia | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences (all) | 0 | 0 | 1 |
| Ileus paralytic | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Oral pain | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Lip dry | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Lip swelling | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nausea | | | |
| subjects affected / exposed | 2 / 13 (15.38%) | 1 / 24 (4.17%) | 6 / 65 (9.23%) |
| occurrences (all) | 6 | 1 | 10 |
| Impaired gastric emptying | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 24 (4.17%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Saliva discolouration | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 1 / 24 (4.17%) | 0 / 65 (0.00%) |
| occurrences (all) | 1 | 5 | 0 |
| Salivary hypersecretion | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 6 / 24 (25.00%) | 10 / 65 (15.38%) |
| occurrences (all) | 1 | 14 | 17 |
| Scalloped tongue | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Teething | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 4 / 24 (16.67%) | 9 / 65 (13.85%) |
| occurrences (all) | 0 | 4 | 10 |
| Toothache | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 2 / 24 (8.33%) | 1 / 65 (1.54%) |
| occurrences (all) | 0 | 2 | 4 |
| Vomiting | | | |
| subjects affected / exposed | 7 / 13 (53.85%) | 9 / 24 (37.50%) | 23 / 65 (35.38%) |
| occurrences (all) | 23 | 21 | 53 |
| Tooth impacted | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hepatobiliary disorders | | | |
| Hepatic steatosis | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 2 / 65 (3.08%) |
| occurrences (all) | 0 | 0 | 2 |

| | | | |
|---|---|---|---|
| Skin and subcutaneous tissue disorders | | | |
| Decubitus ulcer | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 2 / 24 (8.33%) | 3 / 65 (4.62%) |
| occurrences (all) | 0 | 2 | 3 |
| Acne | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Alopecia | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 1 / 24 (4.17%) | 1 / 65 (1.54%) |
| occurrences (all) | 1 | 1 | 1 |
| Blister | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 2 / 24 (8.33%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Dry skin | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dermatitis diaper | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 2 / 24 (8.33%) | 2 / 65 (3.08%) |
| occurrences (all) | 0 | 2 | 2 |
| Dermatitis contact | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 3 / 24 (12.50%) | 3 / 65 (4.62%) |
| occurrences (all) | 0 | 4 | 4 |
| Dermatitis | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ecchymosis | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Keratosis pilaris | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 2 / 24 (8.33%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Erythema | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 1 / 24 (4.17%) | 3 / 65 (4.62%) |
| occurrences (all) | 1 | 1 | 3 |
| Eczema | | | |

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|---|---|---|---|
| subjects affected / exposed | 1 / 13 (7.69%) | 1 / 24 (4.17%) | 2 / 65 (3.08%) |
| occurrences (all) | 1 | 1 | 2 |
| Miliaria | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 3 / 24 (12.50%) | 2 / 65 (3.08%) |
| occurrences (all) | 0 | 4 | 2 |
| Petechiae | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences (all) | 1 | 0 | 1 |
| Photosensitivity reaction | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pruritus | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Rash | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 4 / 24 (16.67%) | 7 / 65 (10.77%) |
| occurrences (all) | 1 | 7 | 8 |
| Scab | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin mass | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 24 (4.17%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Urticaria | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 2 / 24 (8.33%) | 2 / 65 (3.08%) |
| occurrences (all) | 0 | 2 | 3 |
| Renal and urinary disorders | | | |
| Nephrolithiasis | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences (all) | 0 | 0 | 1 |
| Pollakiuria | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 24 (4.17%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Proteinuria | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 24 (4.17%) | 7 / 65 (10.77%) |
| occurrences (all) | 0 | 2 | 11 |

| | | | |
|---|---|---|---|
| Urinary retention | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 1 / 24 (4.17%) | 3 / 65 (4.62%) |
| occurrences (all) | 1 | 1 | 3 |
| Kidney enlargement | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Haematuria | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 1 / 24 (4.17%) | 0 / 65 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Dysuria | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences (all) | 0 | 0 | 1 |
| Endocrine disorders | | | |
| Precocious puberty | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 2 / 24 (8.33%) | 4 / 65 (6.15%) |
| occurrences (all) | 0 | 2 | 5 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 2 / 13 (15.38%) | 3 / 24 (12.50%) | 4 / 65 (6.15%) |
| occurrences (all) | 2 | 3 | 5 |
| Deformity thorax | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Bone pain | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences (all) | 0 | 0 | 1 |
| Back pain | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 2 / 24 (8.33%) | 7 / 65 (10.77%) |
| occurrences (all) | 1 | 4 | 7 |
| Foot deformity | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences (all) | 0 | 0 | 1 |
| Knee deformity | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Joint range of motion decreased | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 13 (0.00%) | 2 / 24 (8.33%) | 2 / 65 (3.08%) |
| occurrences (all) | 0 | 2 | 3 |
| Joint laxity | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences (all) | 0 | 0 | 1 |
| Joint contracture | | | |
| subjects affected / exposed | 4 / 13 (30.77%) | 6 / 24 (25.00%) | 16 / 65 (24.62%) |
| occurrences (all) | 7 | 11 | 26 |
| Hip deformity | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 9 / 65 (13.85%) |
| occurrences (all) | 2 | 0 | 17 |
| Kyphoscoliosis | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 24 (4.17%) | 5 / 65 (7.69%) |
| occurrences (all) | 0 | 2 | 7 |
| Kyphosis | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 10 / 65 (15.38%) |
| occurrences (all) | 1 | 0 | 15 |
| Muscle atrophy | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Muscle spasms | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 3 / 65 (4.62%) |
| occurrences (all) | 0 | 0 | 3 |
| Muscle contracture | | | |
| subjects affected / exposed | 5 / 13 (38.46%) | 6 / 24 (25.00%) | 18 / 65 (27.69%) |
| occurrences (all) | 6 | 8 | 44 |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Limb asymmetry | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal stiffness | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences (all) | 1 | 0 | 1 |
| Pain in extremity | | | |

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|---|---|---|---|
| subjects affected / exposed | 1 / 13 (7.69%) | 4 / 24 (16.67%) | 7 / 65 (10.77%) |
| occurrences (all) | 1 | 5 | 10 |
| Pathological fracture | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences (all) | 0 | 0 | 1 |
| Scoliosis | | | |
| subjects affected / exposed | 6 / 13 (46.15%) | 10 / 24 (41.67%) | 38 / 65 (58.46%) |
| occurrences (all) | 6 | 10 | 60 |
| Spinal deformity | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Neck pain | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Neuromuscular scoliosis | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 24 (4.17%) | 1 / 65 (1.54%) |
| occurrences (all) | 0 | 1 | 2 |
| Osteopenia | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 24 (4.17%) | 9 / 65 (13.85%) |
| occurrences (all) | 0 | 1 | 10 |
| Osteoporosis | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 1 / 24 (4.17%) | 7 / 65 (10.77%) |
| occurrences (all) | 1 | 1 | 7 |
| Tendinous contracture | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 1 / 24 (4.17%) | 1 / 65 (1.54%) |
| occurrences (all) | 2 | 1 | 2 |
| Infections and infestations | | | |
| Abdominal abscess | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Bronchiolitis | | | |
| subjects affected / exposed | 2 / 13 (15.38%) | 0 / 24 (0.00%) | 2 / 65 (3.08%) |
| occurrences (all) | 2 | 0 | 2 |
| Adenovirus infection | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 2 / 24 (8.33%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |

| | | | |
|---|---|---|---|
| Bacterial disease carrier | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 4 / 24 (16.67%) | 4 / 65 (6.15%) |
| occurrences (all) | 0 | 7 | 4 |
| Bacterial infection | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Acute sinusitis | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Coronavirus infection | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 1 / 24 (4.17%) | 2 / 65 (3.08%) |
| occurrences (all) | 1 | 1 | 3 |
| Covid-19 | | | |
| subjects affected / exposed | 4 / 13 (30.77%) | 1 / 24 (4.17%) | 16 / 65 (24.62%) |
| occurrences (all) | 4 | 1 | 18 |
| Coxsackie viral infection | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 24 (4.17%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Conjunctivitis | | | |
| subjects affected / exposed | 2 / 13 (15.38%) | 3 / 24 (12.50%) | 8 / 65 (12.31%) |
| occurrences (all) | 2 | 4 | 10 |
| Bronchitis | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 1 / 24 (4.17%) | 10 / 65 (15.38%) |
| occurrences (all) | 1 | 1 | 15 |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 2 / 24 (8.33%) | 2 / 65 (3.08%) |
| occurrences (all) | 0 | 2 | 2 |
| Clostridium difficile infection | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Croup infectious | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Cystitis | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 24 (4.17%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

| | | | |
|---|---|---|---|
| Ear infection | | | |
| subjects affected / exposed | 2 / 13 (15.38%) | 3 / 24 (12.50%) | 21 / 65 (32.31%) |
| occurrences (all) | 2 | 6 | 31 |
| Ear infection fungal | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 2 / 24 (8.33%) | 1 / 65 (1.54%) |
| occurrences (all) | 0 | 2 | 1 |
| Enterovirus infection | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 4 / 24 (16.67%) | 4 / 65 (6.15%) |
| occurrences (all) | 0 | 6 | 4 |
| Gastroenteritis viral | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 24 (4.17%) | 4 / 65 (6.15%) |
| occurrences (all) | 0 | 1 | 4 |
| Fungal skin infection | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 24 (4.17%) | 2 / 65 (3.08%) |
| occurrences (all) | 0 | 1 | 2 |
| Gastritis viral | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 2 / 24 (8.33%) | 9 / 65 (13.85%) |
| occurrences (all) | 1 | 3 | 10 |
| Eye infection | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 1 / 24 (4.17%) | 0 / 65 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Gastrointestinal viral infection | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences (all) | 0 | 0 | 2 |
| Hand-foot-and-mouth disease | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hordeolum | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 2 / 24 (8.33%) | 4 / 65 (6.15%) |
| occurrences (all) | 0 | 2 | 4 |
| Impetigo | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 2 / 24 (8.33%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |

| | | | |
|---|---|---|---|
| Influenza | | | |
| subjects affected / exposed | 2 / 13 (15.38%) | 3 / 24 (12.50%) | 13 / 65 (20.00%) |
| occurrences (all) | 4 | 3 | 14 |
| Klebsiella infection | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 2 / 24 (8.33%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 3 / 24 (12.50%) | 4 / 65 (6.15%) |
| occurrences (all) | 1 | 3 | 7 |
| Lower respiratory tract infection viral | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Metapneumovirus infection | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences (all) | 1 | 0 | 1 |
| Otitis externa | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 4 / 65 (6.15%) |
| occurrences (all) | 2 | 0 | 8 |
| Oral fungal infection | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 2 / 24 (8.33%) | 1 / 65 (1.54%) |
| occurrences (all) | 0 | 3 | 1 |
| Otitis media | | | |
| subjects affected / exposed | 4 / 13 (30.77%) | 4 / 24 (16.67%) | 14 / 65 (21.54%) |
| occurrences (all) | 7 | 7 | 23 |
| Otitis media acute | | | |
| subjects affected / exposed | 2 / 13 (15.38%) | 2 / 24 (8.33%) | 3 / 65 (4.62%) |
| occurrences (all) | 2 | 2 | 3 |
| Moraxella infection | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 2 / 24 (8.33%) | 2 / 65 (3.08%) |
| occurrences (all) | 0 | 2 | 2 |
| Mycoplasma infection | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 4 / 13 (30.77%) | 5 / 24 (20.83%) | 26 / 65 (40.00%) |
| occurrences (all) | 14 | 20 | 74 |

| | | | |
|---|---|---|---|
| Oral candidiasis | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 3 / 24 (12.50%) | 0 / 65 (0.00%) |
| occurrences (all) | 1 | 3 | 0 |
| Pneumonia | | | |
| subjects affected / exposed | 4 / 13 (30.77%) | 6 / 24 (25.00%) | 18 / 65 (27.69%) |
| occurrences (all) | 9 | 8 | 24 |
| Pharyngitis streptococcal | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 2 / 65 (3.08%) |
| occurrences (all) | 1 | 0 | 3 |
| Pseudomonas infection | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 6 / 24 (25.00%) | 11 / 65 (16.92%) |
| occurrences (all) | 0 | 10 | 17 |
| Parainfluenzae virus infection | | | |
| subjects affected / exposed | 2 / 13 (15.38%) | 0 / 24 (0.00%) | 5 / 65 (7.69%) |
| occurrences (all) | 2 | 0 | 5 |
| Pharyngitis | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 2 / 24 (8.33%) | 4 / 65 (6.15%) |
| occurrences (all) | 0 | 2 | 4 |
| Pneumonia bacterial | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences (all) | 0 | 0 | 1 |
| Postoperative wound infection | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences (all) | 0 | 0 | 1 |
| Respiratory syncytial virus infection | | | |
| subjects affected / exposed | 2 / 13 (15.38%) | 2 / 24 (8.33%) | 8 / 65 (12.31%) |
| occurrences (all) | 3 | 2 | 10 |
| Pneumonia aspiration | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 2 / 24 (8.33%) | 7 / 65 (10.77%) |
| occurrences (all) | 0 | 2 | 8 |
| Respiratory tract infection | | | |
| subjects affected / exposed | 4 / 13 (30.77%) | 2 / 24 (8.33%) | 22 / 65 (33.85%) |
| occurrences (all) | 16 | 4 | 44 |
| Respiratory tract infection viral | | | |
| subjects affected / exposed | 2 / 13 (15.38%) | 1 / 24 (4.17%) | 6 / 65 (9.23%) |
| occurrences (all) | 3 | 1 | 7 |

| | | | |
|---|---|---|---|
| Rhinitis | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 6 / 24 (25.00%) | 5 / 65 (7.69%) |
| occurrences (all) | 0 | 7 | 17 |
| Rhinovirus infection | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 12 / 65 (18.46%) |
| occurrences (all) | 0 | 0 | 20 |
| Serratia infection | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 2 / 24 (8.33%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Sinusitis | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 2 / 24 (8.33%) | 6 / 65 (9.23%) |
| occurrences (all) | 1 | 2 | 6 |
| Staphylococcal infection | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 24 (4.17%) | 7 / 65 (10.77%) |
| occurrences (all) | 0 | 1 | 11 |
| Stenotrophomonas infection | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 2 / 24 (8.33%) | 1 / 65 (1.54%) |
| occurrences (all) | 0 | 2 | 1 |
| Respiratory tract infection bacterial | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Stoma site infection | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 1 / 24 (4.17%) | 4 / 65 (6.15%) |
| occurrences (all) | 1 | 2 | 5 |
| Suspected covid-19 | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tonsillitis | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 1 / 24 (4.17%) | 1 / 65 (1.54%) |
| occurrences (all) | 1 | 1 | 2 |
| Tooth abscess | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Stoma site cellulitis | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 2 / 24 (8.33%) | 2 / 65 (3.08%) |
| occurrences (all) | 0 | 6 | 2 |

| | | | |
|---|---|---|---|
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 11 / 13 (84.62%) | 14 / 24 (58.33%) | 34 / 65 (52.31%) |
| occurrences (all) | 16 | 35 | 109 |
| Upper respiratory tract infection bacterial | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences (all) | 0 | 0 | 1 |
| Urinary tract infection | | | |
| subjects affected / exposed | 3 / 13 (23.08%) | 3 / 24 (12.50%) | 10 / 65 (15.38%) |
| occurrences (all) | 5 | 7 | 20 |
| Tracheitis | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 4 / 24 (16.67%) | 3 / 65 (4.62%) |
| occurrences (all) | 0 | 5 | 8 |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 2 / 13 (15.38%) | 1 / 24 (4.17%) | 5 / 65 (7.69%) |
| occurrences (all) | 3 | 1 | 14 |
| Viral infection | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 1 / 24 (4.17%) | 3 / 65 (4.62%) |
| occurrences (all) | 2 | 1 | 3 |
| Metabolism and nutrition disorders | | | |
| Feeding intolerance | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 1 / 24 (4.17%) | 0 / 65 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Electrolyte imbalance | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences (all) | 0 | 0 | 1 |
| Dehydration | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 2 / 24 (8.33%) | 6 / 65 (9.23%) |
| occurrences (all) | 0 | 3 | 7 |
| Hypocalcaemia | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 2 / 24 (8.33%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Hyponatraemia | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences (all) | 0 | 0 | 1 |
| Hypokalaemia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 13 (7.69%) | 3 / 24 (12.50%) | 10 / 65 (15.38%) |
| occurrences (all) | 1 | 5 | 11 |
| Hypoglycaemia | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 3 / 65 (4.62%) |
| occurrences (all) | 1 | 0 | 4 |
| Hypochloraemia | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences (all) | 0 | 0 | 1 |
| Malnutrition | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 0 / 24 (0.00%) | 6 / 65 (9.23%) |
| occurrences (all) | 1 | 0 | 6 |
| Iron deficiency | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 2 / 24 (8.33%) | 2 / 65 (3.08%) |
| occurrences (all) | 0 | 2 | 2 |
| Hypovolaemia | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 1 / 24 (4.17%) | 1 / 65 (1.54%) |
| occurrences (all) | 0 | 1 | 1 |
| Metabolic acidosis | | | |
| subjects affected / exposed | 2 / 13 (15.38%) | 1 / 24 (4.17%) | 2 / 65 (3.08%) |
| occurrences (all) | 2 | 1 | 2 |
| Obesity | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 1 / 65 (1.54%) |
| occurrences (all) | 0 | 0 | 1 |
| Vitamin d deficiency | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 2 / 65 (3.08%) |
| occurrences (all) | 0 | 0 | 2 |
| Weight gain poor | | | |
| subjects affected / exposed | 1 / 13 (7.69%) | 1 / 24 (4.17%) | 3 / 65 (4.62%) |
| occurrences (all) | 1 | 2 | 3 |
| Metabolic alkalosis | | | |
| subjects affected / exposed | 0 / 13 (0.00%) | 0 / 24 (0.00%) | 0 / 65 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| **Non-serious adverse events** | Infantile SMA Onset 232SM202 | Later SMA Onset 232SM202 | Later SMA Onset CS12 Type 3 |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 12 / 12 (100.00%) | 8 / 8 (100.00%) | 25 / 25 (100.00%) |

| | | | |
|---|---|---|---|
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Skin papilloma | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 2 / 25 (8.00%) |
| occurrences (all) | 0 | 0 | 2 |
| Hair follicle tumour benign | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 2 / 12 (16.67%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Hypotension | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 3 / 12 (25.00%) | 0 / 8 (0.00%) | 3 / 25 (12.00%) |
| occurrences (all) | 3 | 0 | 4 |
| Developmental delay | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gait disturbance | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 3 / 25 (12.00%) |
| occurrences (all) | 0 | 0 | 3 |
| Infusion site bruising | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 8 (12.50%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Medical device site haemorrhage | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Peripheral swelling | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 2 / 25 (8.00%) |
| occurrences (all) | 0 | 0 | 2 |

| | | | |
|---|---|---|---|
| Pneumatosis | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pyrexia | | | |
| subjects affected / exposed | 5 / 12 (41.67%) | 5 / 8 (62.50%) | 3 / 25 (12.00%) |
| occurrences (all) | 15 | 6 | 5 |
| Pain | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 8 (12.50%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Immune system disorders | | | |
| Drug hypersensitivity | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Multiple allergies | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 8 (12.50%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Seasonal allergy | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 2 / 25 (8.00%) |
| occurrences (all) | 0 | 0 | 2 |
| Reproductive system and breast disorders | | | |
| Heavy menstrual bleeding | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 1 / 25 (4.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Testicular atrophy | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute respiratory failure | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Adenoidal hypertrophy | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Aspiration | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

| | | | |
|---|---|---|---|
| Asthma | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 1 / 25 (4.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Atelectasis | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Bronchial wall thickening | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Chronic respiratory failure | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Epiglottic oedema | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Emphysema | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dyspnoea | | | |
| subjects affected / exposed | 2 / 12 (16.67%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Cough | | | |
| subjects affected / exposed | 5 / 12 (41.67%) | 5 / 8 (62.50%) | 2 / 25 (8.00%) |
| occurrences (all) | 7 | 8 | 3 |
| Epistaxis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 3 / 25 (12.00%) |
| occurrences (all) | 0 | 0 | 4 |
| Increased upper airway secretion | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Increased viscosity of upper respiratory secretion | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Increased bronchial secretion | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypoxia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Laryngospasm | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lower respiratory tract congestion | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nasal congestion | | | |
| subjects affected / exposed | 2 / 12 (16.67%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 4 | 0 | 0 |
| Lung infiltration | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pleural effusion | | | |
| subjects affected / exposed | 3 / 12 (25.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Obstructive sleep apnoea syndrome | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Obstructive airways disorder | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Noninfective bronchitis | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 1 / 8 (12.50%) | 3 / 25 (12.00%) |
| occurrences (all) | 2 | 1 | 3 |
| Respiratory disorder | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 1 / 8 (12.50%) | 1 / 25 (4.00%) |
| occurrences (all) | 1 | 1 | 1 |
| Rales | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pulmonary oedema | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Productive cough | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory distress | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Rhinorrhoea | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 2 / 8 (25.00%) | 1 / 25 (4.00%) |
| occurrences (all) | 1 | 2 | 1 |
| Rhinitis allergic | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 8 (12.50%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Restrictive pulmonary disease | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tonsillar hypertrophy | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 1 / 25 (4.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Tachypnoea | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Sputum discoloured | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sleep apnoea syndrome | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Wheezing | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Psychiatric disorders | | | |

| | | | |
|---|---|---|---|
| Anxiety | | | |
| subjects affected / exposed | 2 / 12 (16.67%) | 0 / 8 (0.00%) | 3 / 25 (12.00%) |
| occurrences (all) | 2 | 0 | 3 |
| Agitation | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Anxiety disorder | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Attention deficit hyperactivity disorder | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 1 / 25 (4.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Panic attack | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 2 / 25 (8.00%) |
| occurrences (all) | 0 | 0 | 2 |
| Mental status changes | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Learning disability | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Irritability | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Insomnia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Encopresis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 8 (12.50%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Depression | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 2 / 25 (8.00%) |
| occurrences (all) | 0 | 0 | 2 |
| Product issues | | | |

| | | | |
|---|---|---|---|
| Device malfunction | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Device dislocation | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Investigations | | | |
| Activated partial thromboplastin time prolonged | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood albumin decreased | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Blood iron decreased | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Blood potassium decreased | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Bone density decreased | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Breath sounds abnormal | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cardiac murmur | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Clostridium test positive | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Heart rate increased | | | |
| subjects affected / exposed | 3 / 12 (25.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 5 | 0 | 0 |
| Electrocardiogram qt prolonged | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gamma-glutamyltransferase increased | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Haemoglobin decreased | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Crystal urine present | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oxygen consumption decreased | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Occult blood positive | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Mean platelet volume decreased | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Oxygen saturation decreased | | | |
| subjects affected / exposed | 2 / 12 (16.67%) | 0 / 8 (0.00%) | 1 / 25 (4.00%) |
| occurrences (all) | 3 | 0 | 1 |
| Qrs axis abnormal | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pseudomonas test positive | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Prothrombin time prolonged | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Platelet count increased | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

| | | | |
|---|---|---|---|
| Red blood cell count increased | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Red blood cell sedimentation rate increased | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Sars-cov-2 test positive | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 1 / 25 (4.00%) |
| occurrences (all) | 1 | 0 | 1 |
| Vitamin d decreased | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 1 / 25 (4.00%) |
| occurrences (all) | 0 | 0 | 1 |
| White blood cells urine positive | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Weight increased | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Weight decreased | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 1 / 25 (4.00%) |
| occurrences (all) | 1 | 0 | 1 |
| Von willebrand\'s factor activity decreased | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| White blood cell count increased | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| Contusion | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Arthropod bite | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Concussion | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 2 / 25 (8.00%) |
| occurrences (all) | 0 | 0 | 2 |
| Anaesthetic complication neurological | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Anaesthetic complication | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 1 / 25 (4.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Accident | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Femur fracture | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 2 / 8 (25.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 2 | 3 | 0 |
| Fibula fracture | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrointestinal stoma complication | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Humerus fracture | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Fall | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 6 / 25 (24.00%) |
| occurrences (all) | 0 | 0 | 10 |
| Incision site swelling | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Endotracheal intubation complication | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Extraskeletal ossification | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

| | | | |
|---|---|---|---|
| Immunisation reaction | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 8 (12.50%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Post procedural contusion | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Post procedural constipation | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Post procedural complication | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Post lumbar puncture syndrome | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 2 / 8 (25.00%) | 15 / 25 (60.00%) |
| occurrences (all) | 0 | 2 | 34 |
| Palate injury | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lower limb fracture | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 1 / 8 (12.50%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Post procedural haemorrhage | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 1 / 25 (4.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Ligament sprain | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 1 / 8 (12.50%) | 5 / 25 (20.00%) |
| occurrences (all) | 1 | 1 | 5 |
| Joint dislocation | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Post procedural inflammation | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Procedural hypotension | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

| | | | |
|---|---|---|---|
| Procedural pain | | | |
| subjects affected / exposed | 2 / 12 (16.67%) | 2 / 8 (25.00%) | 11 / 25 (44.00%) |
| occurrences (all) | 2 | 4 | 34 |
| Procedural pneumothorax | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Procedural vomiting | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory tract procedural complication | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Skin abrasion | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Stoma site discharge | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Stoma site erythema | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Stoma site haemorrhage | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Stoma site hypergranulation | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Suture rupture | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 8 (12.50%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Tibia fracture | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tooth fracture | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Wound dehiscence | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Wound secretion | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Congenital, familial and genetic disorders | | | |
| Developmental hip dysplasia | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 1 / 8 (12.50%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Cryptorchism | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| High arched palate | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cardiac disorders | | | |
| Bradycardia | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Tachycardia | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Sinus tachycardia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Right ventricular hypertrophy | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Right atrial enlargement | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pericardial effusion | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nervous system disorders | | | |
| Areflexia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dizziness | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 2 / 25 (8.00%) |
| occurrences (all) | 0 | 0 | 2 |
| Cognitive disorder | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Disturbance in attention | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Autonomic nervous system imbalance | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dysarthria | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Migraine | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 2 / 25 (8.00%) |
| occurrences (all) | 0 | 0 | 2 |
| Lethargy | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Intracranial pressure increased | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 1 / 8 (12.50%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Hyporeflexia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Horner\'s syndrome | | | |

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|---|---|---|---|
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Headache | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 3 / 8 (37.50%) | 17 / 25 (68.00%) |
| occurrences (all) | 1 | 5 | 47 |
| Motor developmental delay | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Paraesthesia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 8 (12.50%) | 1 / 25 (4.00%) |
| occurrences (all) | 0 | 1 | 1 |
| Nystagmus | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Myoclonus | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Muscle contractions involuntary | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 1 / 25 (4.00%) |
| occurrences (all) | 1 | 0 | 1 |
| Tremor | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 1 / 25 (4.00%) |
| occurrences (all) | 0 | 0 | 2 |
| Blood and lymphatic system disorders | | | |
| Thrombocytosis | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Thrombocytopenia | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Lymphadenopathy | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Leukocytosis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Iron deficiency anaemia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Anaemia | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 1 / 8 (12.50%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Ear and labyrinth disorders | | | |
| Cerumen impaction | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Ear pain | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 2 / 25 (8.00%) |
| occurrences (all) | 0 | 0 | 2 |
| Hyperacusis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Myringosclerosis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Motion sickness | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 8 (12.50%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Eye disorders | | | |
| Amblyopia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Astigmatism | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 8 (12.50%) | 1 / 25 (4.00%) |
| occurrences (all) | 0 | 1 | 1 |
| Chalazion | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eyelid cyst | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypermetropia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Strabismus | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Myopia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrointestinal disorders | | | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Abdominal distension | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 1 / 25 (4.00%) |
| occurrences (all) | 1 | 0 | 1 |
| Colitis ulcerative | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Constipation | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 3 / 8 (37.50%) | 1 / 25 (4.00%) |
| occurrences (all) | 3 | 3 | 1 |
| Diarrhoea | | | |
| subjects affected / exposed | 2 / 12 (16.67%) | 2 / 8 (25.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 3 | 2 | 0 |
| Dyspepsia | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 1 / 25 (4.00%) |
| occurrences (all) | 1 | 0 | 1 |
| Gastrointestinal motility disorder | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastritis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 1 / 25 (4.00%) |
| occurrences (all) | 0 | 0 | 1 |

| | | | |
|---|---|---|---|
| Gastritis haemorrhagic | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dysphagia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hiatus hernia | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Ileus paralytic | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oral pain | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lip dry | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lip swelling | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Nausea | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 2 / 25 (8.00%) |
| occurrences (all) | 0 | 0 | 3 |
| Impaired gastric emptying | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Saliva discolouration | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Salivary hypersecretion | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Scalloped tongue | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Teething | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Toothache | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vomiting | | | |
| subjects affected / exposed | 3 / 12 (25.00%) | 4 / 8 (50.00%) | 4 / 25 (16.00%) |
| occurrences (all) | 6 | 5 | 15 |
| Tooth impacted | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hepatobiliary disorders | | | |
| Hepatic steatosis | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| Decubitus ulcer | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Acne | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 3 / 25 (12.00%) |
| occurrences (all) | 0 | 0 | 4 |
| Alopecia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blister | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dry skin | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Dermatitis diaper | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dermatitis contact | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dermatitis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 8 (12.50%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Ecchymosis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Keratosis pilaris | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Erythema | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eczema | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Miliaria | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Petechiae | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Photosensitivity reaction | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pruritus | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 1 / 25 (4.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Rash | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Scab | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Skin mass | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urticaria | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Renal and urinary disorders | | | |
| Nephrolithiasis | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pollakiuria | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Proteinuria | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 2 / 25 (8.00%) |
| occurrences (all) | 1 | 0 | 2 |
| Urinary retention | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Kidney enlargement | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Haematuria | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dysuria | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 8 (12.50%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Endocrine disorders | | | |
| Precocious puberty | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 2 / 12 (16.67%) | 0 / 8 (0.00%) | 3 / 25 (12.00%) |
| occurrences (all) | 2 | 0 | 3 |
| Deformity thorax | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Bone pain | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Back pain | | | |
| subjects affected / exposed | 2 / 12 (16.67%) | 1 / 8 (12.50%) | 11 / 25 (44.00%) |
| occurrences (all) | 2 | 1 | 15 |
| Foot deformity | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 1 / 25 (4.00%) |
| occurrences (all) | 1 | 0 | 1 |
| Knee deformity | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Joint range of motion decreased | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Joint laxity | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Joint contracture | | | |
| subjects affected / exposed | 2 / 12 (16.67%) | 1 / 8 (12.50%) | 3 / 25 (12.00%) |
| occurrences (all) | 2 | 1 | 3 |
| Hip deformity | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 2 / 8 (25.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 4 | 0 |
| Kyphoscoliosis | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Kyphosis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 8 (12.50%) | 1 / 25 (4.00%) |
| occurrences (all) | 0 | 1 | 1 |
| Muscle atrophy | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Muscle spasms | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Muscle contracture | | | |
| subjects affected / exposed | 2 / 12 (16.67%) | 1 / 8 (12.50%) | 1 / 25 (4.00%) |
| occurrences (all) | 2 | 1 | 2 |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 1 / 25 (4.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Limb asymmetry | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal stiffness | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pain in extremity | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 1 / 8 (12.50%) | 6 / 25 (24.00%) |
| occurrences (all) | 2 | 1 | 11 |
| Pathological fracture | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Scoliosis | | | |
| subjects affected / exposed | 3 / 12 (25.00%) | 5 / 8 (62.50%) | 2 / 25 (8.00%) |
| occurrences (all) | 3 | 8 | 2 |
| Spinal deformity | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Neck pain | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Neuromuscular scoliosis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Osteopenia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Osteoporosis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 2 / 8 (25.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Tendinous contracture | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infections and infestations | | | |
| Abdominal abscess | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Bronchiolitis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Adenovirus infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Bacterial disease carrier | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Bacterial infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Acute sinusitis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Coronavirus infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Covid-19 | | | |
| subjects affected / exposed | 5 / 12 (41.67%) | 2 / 8 (25.00%) | 5 / 25 (20.00%) |
| occurrences (all) | 6 | 3 | 6 |
| Coxsackie viral infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 8 (12.50%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Conjunctivitis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Bronchitis | | | |
| subjects affected / exposed | 2 / 12 (16.67%) | 1 / 8 (12.50%) | 0 / 25 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Clostridium difficile infection | | | |
| subjects affected / exposed | 2 / 12 (16.67%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Croup infectious | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cystitis | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Ear infection | | | |
| subjects affected / exposed | 2 / 12 (16.67%) | 1 / 8 (12.50%) | 1 / 25 (4.00%) |
| occurrences (all) | 2 | 1 | 1 |
| Ear infection fungal | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Enterovirus infection | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Gastroenteritis viral | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 1 / 8 (12.50%) | 5 / 25 (20.00%) |
| occurrences (all) | 1 | 1 | 5 |

| | | | |
|---|---|---|---|
| Fungal skin infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastritis viral | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 2 / 12 (16.67%) | 1 / 8 (12.50%) | 0 / 25 (0.00%) |
| occurrences (all) | 2 | 3 | 0 |
| Eye infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrointestinal viral infection | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hand-foot-and-mouth disease | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hordeolum | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Impetigo | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Influenza | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 8 (12.50%) | 3 / 25 (12.00%) |
| occurrences (all) | 0 | 1 | 4 |
| Klebsiella infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 8 (12.50%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Lower respiratory tract infection viral | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 8 (12.50%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

| | | | |
|---|---|---|---|
| Metapneumovirus infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Otitis externa | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Oral fungal infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Otitis media | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 1 / 8 (12.50%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Otitis media acute | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Moraxella infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Mycoplasma infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 4 / 12 (33.33%) | 1 / 8 (12.50%) | 8 / 25 (32.00%) |
| occurrences (all) | 5 | 1 | 10 |
| Oral candidiasis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pneumonia | | | |
| subjects affected / exposed | 4 / 12 (33.33%) | 1 / 8 (12.50%) | 0 / 25 (0.00%) |
| occurrences (all) | 5 | 3 | 0 |
| Pharyngitis streptococcal | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 8 (12.50%) | 3 / 25 (12.00%) |
| occurrences (all) | 0 | 1 | 3 |
| Pseudomonas infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Parainfluenzae virus infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pharyngitis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pneumonia bacterial | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Postoperative wound infection | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Respiratory syncytial virus infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 8 (12.50%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pneumonia aspiration | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory tract infection | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 2 / 8 (25.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 3 | 0 |
| Respiratory tract infection viral | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 2 / 8 (25.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 4 | 0 |
| Rhinitis | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Rhinovirus infection | | | |
| subjects affected / exposed | 2 / 12 (16.67%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Serratia infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sinusitis | | | |
| subjects affected / exposed | 2 / 12 (16.67%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |

| | | | |
|---|---|---|---|
| Staphylococcal infection | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Stenotrophomonas infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory tract infection bacterial | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Stoma site infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Suspected covid-19 | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tonsillitis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 1 / 25 (4.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Tooth abscess | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Stoma site cellulitis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 3 / 12 (25.00%) | 6 / 8 (75.00%) | 5 / 25 (20.00%) |
| occurrences (all) | 6 | 18 | 10 |
| Upper respiratory tract infection bacterial | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Urinary tract infection | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 1 / 8 (12.50%) | 1 / 25 (4.00%) |
| occurrences (all) | 2 | 1 | 3 |
| Tracheitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 2 / 25 (8.00%) |
| occurrences (all) | 0 | 0 | 2 |
| Viral infection | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 8 (12.50%) | 4 / 25 (16.00%) |
| occurrences (all) | 0 | 2 | 5 |
| Metabolism and nutrition disorders | | | |
| Feeding intolerance | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Electrolyte imbalance | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Dehydration | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 1 / 25 (4.00%) |
| occurrences (all) | 2 | 0 | 1 |
| Hypocalcaemia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyponatraemia | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hypokalaemia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypoglycaemia | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypochloraemia | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Malnutrition | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Iron deficiency | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypovolaemia | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Metabolic acidosis | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Obesity | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 2 / 25 (8.00%) |
| occurrences (all) | 0 | 0 | 2 |
| Vitamin d deficiency | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 1 / 8 (12.50%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Weight gain poor | | | |
| subjects affected / exposed | 0 / 12 (0.00%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Metabolic alkalosis | | | |
| subjects affected / exposed | 1 / 12 (8.33%) | 0 / 8 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

| **Non-serious adverse events** | Later SMA Onset CS12 Type 2 | Later SMA Onset CS4 Previous Control | Later SMA Onset CS4 Previous ISIS 396443 |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 20 / 20 (100.00%) | 40 / 42 (95.24%) | 79 / 83 (95.18%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Skin papilloma | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 42 (2.38%) | 1 / 83 (1.20%) |
| occurrences (all) | 0 | 1 | 1 |
| Hair follicle tumour benign | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 1 / 83 (1.20%) |
| occurrences (all) | 0 | 0 | 2 |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Hypotension | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 1 / 42 (2.38%) | 1 / 83 (1.20%) |
| occurrences (all) | 1 | 1 | 1 |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 1 / 83 (1.20%) |
| occurrences (all) | 0 | 0 | 1 |
| Developmental delay | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gait disturbance | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infusion site bruising | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Medical device site haemorrhage | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Peripheral swelling | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 42 (2.38%) | 2 / 83 (2.41%) |
| occurrences (all) | 0 | 1 | 2 |
| Pneumatosis | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pyrexia | | | |
| subjects affected / exposed | 10 / 20 (50.00%) | 21 / 42 (50.00%) | 39 / 83 (46.99%) |
| occurrences (all) | 21 | 55 | 117 |
| Pain | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 42 (2.38%) | 2 / 83 (2.41%) |
| occurrences (all) | 0 | 1 | 2 |
| Immune system disorders | | | |

| | | | |
|---|---|---|---|
| Drug hypersensitivity | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 1 / 42 (2.38%) | 2 / 83 (2.41%) |
| occurrences (all) | 1 | 1 | 2 |
| Multiple allergies | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 1 / 83 (1.20%) |
| occurrences (all) | 0 | 0 | 1 |
| Seasonal allergy | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 3 / 42 (7.14%) | 5 / 83 (6.02%) |
| occurrences (all) | 1 | 3 | 6 |
| Reproductive system and breast disorders | | | |
| Heavy menstrual bleeding | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Testicular atrophy | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute respiratory failure | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 1 / 83 (1.20%) |
| occurrences (all) | 0 | 0 | 2 |
| Adenoidal hypertrophy | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 42 (0.00%) | 1 / 83 (1.20%) |
| occurrences (all) | 1 | 0 | 1 |
| Aspiration | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Asthma | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 3 / 42 (7.14%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Atelectasis | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 2 / 83 (2.41%) |
| occurrences (all) | 0 | 0 | 3 |
| Bronchial wall thickening | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Chronic respiratory failure | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Epiglottic oedema | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Emphysema | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 1 / 83 (1.20%) |
| occurrences (all) | 0 | 0 | 1 |
| Cough | | | |
| subjects affected / exposed | 6 / 20 (30.00%) | 15 / 42 (35.71%) | 29 / 83 (34.94%) |
| occurrences (all) | 7 | 33 | 62 |
| Epistaxis | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 42 (2.38%) | 2 / 83 (2.41%) |
| occurrences (all) | 0 | 1 | 3 |
| Increased upper airway secretion | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 1 / 83 (1.20%) |
| occurrences (all) | 0 | 0 | 1 |
| Increased viscosity of upper respiratory secretion | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Increased bronchial secretion | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 1 / 83 (1.20%) |
| occurrences (all) | 0 | 0 | 1 |
| Hypoxia | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 42 (0.00%) | 2 / 83 (2.41%) |
| occurrences (all) | 1 | 0 | 2 |
| Laryngospasm | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 42 (0.00%) | 1 / 83 (1.20%) |
| occurrences (all) | 1 | 0 | 1 |
| Lower respiratory tract congestion | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 1 / 83 (1.20%) |
| occurrences (all) | 0 | 0 | 1 |

| | | | |
|---|---|---|---|
| Nasal congestion | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 1 / 42 (2.38%) | 9 / 83 (10.84%) |
| occurrences (all) | 1 | 3 | 12 |
| Lung infiltration | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 1 / 83 (1.20%) |
| occurrences (all) | 0 | 0 | 1 |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 42 (2.38%) | 1 / 83 (1.20%) |
| occurrences (all) | 0 | 1 | 1 |
| Obstructive sleep apnoea syndrome | | | |
| subjects affected / exposed | 2 / 20 (10.00%) | 4 / 42 (9.52%) | 5 / 83 (6.02%) |
| occurrences (all) | 2 | 5 | 5 |
| Obstructive airways disorder | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Noninfective bronchitis | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 4 / 20 (20.00%) | 8 / 42 (19.05%) | 12 / 83 (14.46%) |
| occurrences (all) | 5 | 9 | 27 |
| Respiratory disorder | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 1 / 83 (1.20%) |
| occurrences (all) | 0 | 0 | 2 |
| Rales | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pulmonary oedema | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 42 (2.38%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Productive cough | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 2 / 42 (4.76%) | 5 / 83 (6.02%) |
| occurrences (all) | 1 | 3 | 8 |
| Respiratory distress | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 1 / 83 (1.20%) |
| occurrences (all) | 0 | 0 | 1 |

| | | | |
|---|---|---|---|
| Rhinorrhoea | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 4 / 42 (9.52%) | 8 / 83 (9.64%) |
| occurrences (all) | 1 | 7 | 13 |
| Rhinitis allergic | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 3 / 42 (7.14%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 4 | 0 |
| Restrictive pulmonary disease | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 1 / 42 (2.38%) | 2 / 83 (2.41%) |
| occurrences (all) | 1 | 1 | 2 |
| Tonsillar hypertrophy | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 42 (2.38%) | 3 / 83 (3.61%) |
| occurrences (all) | 0 | 1 | 3 |
| Tachypnoea | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sputum discoloured | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sleep apnoea syndrome | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 3 / 42 (7.14%) | 1 / 83 (1.20%) |
| occurrences (all) | 0 | 3 | 1 |
| Wheezing | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 2 / 42 (4.76%) | 1 / 83 (1.20%) |
| occurrences (all) | 0 | 2 | 1 |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 3 / 20 (15.00%) | 1 / 42 (2.38%) | 4 / 83 (4.82%) |
| occurrences (all) | 3 | 3 | 4 |
| Agitation | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 42 (2.38%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Anxiety disorder | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Attention deficit hyperactivity disorder | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 42 (2.38%) | 1 / 83 (1.20%) |
| occurrences (all) | 0 | 1 | 1 |
| Panic attack | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Mental status changes | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Learning disability | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Irritability | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 1 / 83 (1.20%) |
| occurrences (all) | 0 | 0 | 1 |
| Insomnia | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 42 (2.38%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Encopresis | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Depression | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Product issues | | | |
| Device malfunction | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Device dislocation | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Investigations | | | |
| Activated partial thromboplastin time prolonged | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 2 / 83 (2.41%) |
| occurrences (all) | 0 | 0 | 2 |
| Blood albumin decreased | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood iron decreased | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood potassium decreased | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Bone density decreased | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 3 / 42 (7.14%) | 1 / 83 (1.20%) |
| occurrences (all) | 1 | 3 | 1 |
| Breath sounds abnormal | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 1 / 83 (1.20%) |
| occurrences (all) | 0 | 0 | 1 |
| Cardiac murmur | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 42 (2.38%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Clostridium test positive | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Heart rate increased | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 2 / 42 (4.76%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Electrocardiogram qt prolonged | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gamma-glutamyltransferase increased | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Haemoglobin decreased | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Crystal urine present | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 4 / 42 (9.52%) | 6 / 83 (7.23%) |
| occurrences (all) | 0 | 4 | 7 |

| | | | |
|---|---|---|---|
| Oxygen consumption decreased | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Occult blood positive | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Mean platelet volume decreased | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oxygen saturation decreased | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 2 / 42 (4.76%) | 3 / 83 (3.61%) |
| occurrences (all) | 0 | 2 | 3 |
| Qrs axis abnormal | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pseudomonas test positive | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Prothrombin time prolonged | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Platelet count increased | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Red blood cell count increased | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Red blood cell sedimentation rate increased | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sars-cov-2 test positive | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 42 (2.38%) | 1 / 83 (1.20%) |
| occurrences (all) | 0 | 1 | 1 |
| Vitamin d decreased | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 20 (5.00%) | 1 / 42 (2.38%) | 1 / 83 (1.20%) |
| occurrences (all) | 1 | 1 | 1 |
| White blood cells urine positive | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 1 / 83 (1.20%) |
| occurrences (all) | 0 | 0 | 1 |
| Weight increased | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 5 / 42 (11.90%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 6 | 0 |
| Weight decreased | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 42 (2.38%) | 3 / 83 (3.61%) |
| occurrences (all) | 0 | 1 | 3 |
| Von willebrand\'s factor activity decreased | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| White blood cell count increased | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| Contusion | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 2 / 42 (4.76%) | 6 / 83 (7.23%) |
| occurrences (all) | 0 | 2 | 6 |
| Arthropod bite | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 2 / 42 (4.76%) | 3 / 83 (3.61%) |
| occurrences (all) | 0 | 2 | 3 |
| Concussion | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 42 (0.00%) | 1 / 83 (1.20%) |
| occurrences (all) | 1 | 0 | 1 |
| Anaesthetic complication neurological | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 1 / 42 (2.38%) | 0 / 83 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Anaesthetic complication | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 42 (0.00%) | 1 / 83 (1.20%) |
| occurrences (all) | 1 | 0 | 1 |
| Accident | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 20 (5.00%) | 2 / 42 (4.76%) | 1 / 83 (1.20%) |
| occurrences (all) | 1 | 2 | 1 |
| Femur fracture | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 5 / 42 (11.90%) | 8 / 83 (9.64%) |
| occurrences (all) | 1 | 5 | 8 |
| Fibula fracture | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Gastrointestinal stoma complication | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Humerus fracture | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 2 / 42 (4.76%) | 3 / 83 (3.61%) |
| occurrences (all) | 0 | 2 | 3 |
| Fall | | | |
| subjects affected / exposed | 3 / 20 (15.00%) | 9 / 42 (21.43%) | 19 / 83 (22.89%) |
| occurrences (all) | 3 | 14 | 23 |
| Incision site swelling | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Endotracheal intubation complication | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Extraskeletal ossification | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Immunisation reaction | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 1 / 83 (1.20%) |
| occurrences (all) | 0 | 0 | 1 |
| Post procedural contusion | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Post procedural constipation | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Post procedural complication | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 2 / 83 (2.41%) |
| occurrences (all) | 0 | 0 | 2 |
| Post lumbar puncture syndrome | | | |
| subjects affected / exposed | 13 / 20 (65.00%) | 7 / 42 (16.67%) | 21 / 83 (25.30%) |
| occurrences (all) | 21 | 18 | 34 |
| Palate injury | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lower limb fracture | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Post procedural haemorrhage | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 42 (2.38%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Ligament sprain | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 1 / 42 (2.38%) | 4 / 83 (4.82%) |
| occurrences (all) | 1 | 1 | 4 |
| Joint dislocation | | | |
| subjects affected / exposed | 2 / 20 (10.00%) | 3 / 42 (7.14%) | 3 / 83 (3.61%) |
| occurrences (all) | 2 | 3 | 3 |
| Post procedural inflammation | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Procedural hypotension | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 1 / 83 (1.20%) |
| occurrences (all) | 0 | 0 | 1 |
| Procedural pain | | | |
| subjects affected / exposed | 6 / 20 (30.00%) | 19 / 42 (45.24%) | 29 / 83 (34.94%) |
| occurrences (all) | 12 | 32 | 55 |
| Procedural pneumothorax | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Procedural vomiting | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 42 (2.38%) | 3 / 83 (3.61%) |
| occurrences (all) | 0 | 1 | 3 |
| Respiratory tract procedural | | | |

| | | | |
|---|---|---|---|
| complication | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 42 (2.38%) | 1 / 83 (1.20%) |
| occurrences (all) | 0 | 1 | 1 |
| Skin abrasion | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 1 / 83 (1.20%) |
| occurrences (all) | 0 | 0 | 1 |
| Stoma site discharge | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Stoma site erythema | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Stoma site haemorrhage | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Stoma site hypergranulation | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Suture rupture | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tibia fracture | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 2 / 42 (4.76%) | 4 / 83 (4.82%) |
| occurrences (all) | 1 | 2 | 4 |
| Tooth fracture | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 42 (0.00%) | 3 / 83 (3.61%) |
| occurrences (all) | 1 | 0 | 3 |
| Wound dehiscence | | | |
| subjects affected / exposed | 2 / 20 (10.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Wound secretion | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Congenital, familial and genetic disorders | | | |

| | | | |
|---|---|---|---|
| Developmental hip dysplasia | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 1 / 42 (2.38%) | 5 / 83 (6.02%) |
| occurrences (all) | 1 | 3 | 5 |
| Cryptorchism | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| High arched palate | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cardiac disorders | | | |
| Bradycardia | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 42 (2.38%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Tachycardia | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 42 (2.38%) | 2 / 83 (2.41%) |
| occurrences (all) | 0 | 1 | 2 |
| Sinus tachycardia | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 42 (2.38%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Right ventricular hypertrophy | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Right atrial enlargement | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pericardial effusion | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nervous system disorders | | | |
| Areflexia | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 1 / 42 (2.38%) | 1 / 83 (1.20%) |
| occurrences (all) | 1 | 1 | 1 |
| Dizziness | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 42 (2.38%) | 2 / 83 (2.41%) |
| occurrences (all) | 0 | 1 | 2 |
| Cognitive disorder | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Disturbance in attention | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Autonomic nervous system imbalance | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dysarthria | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Migraine | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 2 / 42 (4.76%) | 1 / 83 (1.20%) |
| occurrences (all) | 0 | 2 | 1 |
| Lethargy | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 42 (2.38%) | 1 / 83 (1.20%) |
| occurrences (all) | 0 | 1 | 1 |
| Intracranial pressure increased | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyporeflexia | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Horner\'s syndrome | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Headache | | | |
| subjects affected / exposed | 5 / 20 (25.00%) | 20 / 42 (47.62%) | 24 / 83 (28.92%) |
| occurrences (all) | 14 | 38 | 53 |
| Motor developmental delay | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 42 (0.00%) | 1 / 83 (1.20%) |
| occurrences (all) | 1 | 0 | 1 |
| Paraesthesia | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 1 / 83 (1.20%) |
| occurrences (all) | 0 | 0 | 1 |

| | | | |
|---|---|---|---|
| Nystagmus | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Myoclonus | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Muscle contractions involuntary | | | |
| subjects affected / exposed | 2 / 20 (10.00%) | 1 / 42 (2.38%) | 4 / 83 (4.82%) |
| occurrences (all) | 2 | 1 | 4 |
| Tremor | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 1 / 42 (2.38%) | 3 / 83 (3.61%) |
| occurrences (all) | 1 | 1 | 3 |
| Blood and lymphatic system disorders | | | |
| Thrombocytosis | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Thrombocytopenia | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lymphadenopathy | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Leukocytosis | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 42 (2.38%) | 2 / 83 (2.41%) |
| occurrences (all) | 0 | 1 | 2 |
| Iron deficiency anaemia | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 42 (2.38%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Anaemia | | | |
| subjects affected / exposed | 2 / 20 (10.00%) | 1 / 42 (2.38%) | 1 / 83 (1.20%) |
| occurrences (all) | 4 | 1 | 1 |
| Ear and labyrinth disorders | | | |
| Cerumen impaction | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 1 / 83 (1.20%) |
| occurrences (all) | 0 | 0 | 1 |
| Ear pain | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 4 / 83 (4.82%) |
| occurrences (all) | 0 | 0 | 5 |
| Hyperacusis | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Myringosclerosis | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Motion sickness | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 42 (2.38%) | 1 / 83 (1.20%) |
| occurrences (all) | 0 | 1 | 1 |
| Eye disorders | | | |
| Amblyopia | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Astigmatism | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 1 / 83 (1.20%) |
| occurrences (all) | 0 | 0 | 1 |
| Chalazion | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eyelid cyst | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypermetropia | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Strabismus | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Myopia | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 3 / 42 (7.14%) | 4 / 83 (4.82%) |
| occurrences (all) | 0 | 3 | 4 |
| Gastrointestinal disorders | | | |
| Abdominal pain upper | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 20 (0.00%) | 3 / 42 (7.14%) | 5 / 83 (6.02%) |
| occurrences (all) | 0 | 4 | 7 |
| Abdominal distension | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 2 / 42 (4.76%) | 2 / 83 (2.41%) |
| occurrences (all) | 0 | 4 | 2 |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 3 / 42 (7.14%) | 7 / 83 (8.43%) |
| occurrences (all) | 0 | 3 | 7 |
| Colitis ulcerative | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Constipation | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 9 / 42 (21.43%) | 11 / 83 (13.25%) |
| occurrences (all) | 1 | 10 | 11 |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 6 / 42 (14.29%) | 11 / 83 (13.25%) |
| occurrences (all) | 1 | 6 | 13 |
| Dyspepsia | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 1 / 83 (1.20%) |
| occurrences (all) | 0 | 0 | 1 |
| Gastrointestinal motility disorder | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Gastritis | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 2 / 83 (2.41%) |
| occurrences (all) | 0 | 0 | 2 |
| Gastritis haemorrhagic | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dysphagia | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 2 / 42 (4.76%) | 0 / 83 (0.00%) |
| occurrences (all) | 1 | 3 | 0 |
| Gastrooesophageal reflux disease | | | |

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|---|---|---|---|
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 42 (0.00%) | 1 / 83 (1.20%) |
| occurrences (all) | 1 | 0 | 1 |
| Hiatus hernia | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ileus paralytic | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oral pain | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lip dry | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lip swelling | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nausea | | | |
| subjects affected / exposed | 2 / 20 (10.00%) | 8 / 42 (19.05%) | 15 / 83 (18.07%) |
| occurrences (all) | 2 | 11 | 18 |
| Impaired gastric emptying | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Saliva discolouration | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Salivary hypersecretion | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 1 / 83 (1.20%) |
| occurrences (all) | 0 | 0 | 1 |
| Scalloped tongue | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Teething | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Toothache | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 1 / 83 (1.20%) |
| occurrences (all) | 0 | 0 | 1 |
| Vomiting | | | |
| subjects affected / exposed | 7 / 20 (35.00%) | 18 / 42 (42.86%) | 35 / 83 (42.17%) |
| occurrences (all) | 18 | 35 | 64 |
| Tooth impacted | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hepatobiliary disorders | | | |
| Hepatic steatosis | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| Decubitus ulcer | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 1 / 83 (1.20%) |
| occurrences (all) | 0 | 0 | 1 |
| Acne | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 2 / 83 (2.41%) |
| occurrences (all) | 0 | 0 | 2 |
| Alopecia | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blister | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 42 (2.38%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Dry skin | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dermatitis diaper | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dermatitis contact | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 42 (0.00%) | 4 / 83 (4.82%) |
| occurrences (all) | 1 | 0 | 4 |
| Dermatitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ecchymosis | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 42 (0.00%) | 2 / 83 (2.41%) |
| occurrences (all) | 1 | 0 | 2 |
| Keratosis pilaris | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Erythema | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eczema | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 4 / 42 (9.52%) | 2 / 83 (2.41%) |
| occurrences (all) | 0 | 6 | 2 |
| Miliaria | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 1 / 42 (2.38%) | 0 / 83 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Petechiae | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Photosensitivity reaction | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pruritus | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 3 / 83 (3.61%) |
| occurrences (all) | 0 | 0 | 5 |
| Rash | | | |
| subjects affected / exposed | 2 / 20 (10.00%) | 6 / 42 (14.29%) | 8 / 83 (9.64%) |
| occurrences (all) | 2 | 7 | 10 |
| Scab | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Skin mass | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Urticaria | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 20 (0.00%) | 3 / 42 (7.14%) | 6 / 83 (7.23%) |
| occurrences (all) | 0 | 3 | 9 |
| Renal and urinary disorders | | | |
| Nephrolithiasis | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 2 / 83 (2.41%) |
| occurrences (all) | 0 | 0 | 2 |
| Pollakiuria | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 1 / 42 (2.38%) | 3 / 83 (3.61%) |
| occurrences (all) | 1 | 2 | 4 |
| Proteinuria | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 2 / 42 (4.76%) | 8 / 83 (9.64%) |
| occurrences (all) | 0 | 4 | 14 |
| Urinary retention | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 1 / 83 (1.20%) |
| occurrences (all) | 0 | 0 | 1 |
| Kidney enlargement | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Haematuria | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 2 / 83 (2.41%) |
| occurrences (all) | 0 | 0 | 4 |
| Dysuria | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 42 (2.38%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Endocrine disorders | | | |
| Precocious puberty | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 1 / 42 (2.38%) | 0 / 83 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 3 / 20 (15.00%) | 5 / 42 (11.90%) | 6 / 83 (7.23%) |
| occurrences (all) | 6 | 5 | 7 |
| Deformity thorax | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Bone pain | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 20 (5.00%) | 1 / 42 (2.38%) | 0 / 83 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Back pain | | | |
| subjects affected / exposed | 3 / 20 (15.00%) | 11 / 42 (26.19%) | 15 / 83 (18.07%) |
| occurrences (all) | 3 | 14 | 16 |
| Foot deformity | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 3 / 83 (3.61%) |
| occurrences (all) | 0 | 0 | 4 |
| Knee deformity | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Joint range of motion decreased | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 42 (2.38%) | 2 / 83 (2.41%) |
| occurrences (all) | 0 | 1 | 2 |
| Joint laxity | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Joint contracture | | | |
| subjects affected / exposed | 8 / 20 (40.00%) | 11 / 42 (26.19%) | 21 / 83 (25.30%) |
| occurrences (all) | 13 | 16 | 38 |
| Hip deformity | | | |
| subjects affected / exposed | 2 / 20 (10.00%) | 1 / 42 (2.38%) | 2 / 83 (2.41%) |
| occurrences (all) | 2 | 1 | 3 |
| Kyphoscoliosis | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 42 (2.38%) | 3 / 83 (3.61%) |
| occurrences (all) | 0 | 1 | 6 |
| Kyphosis | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 2 / 42 (4.76%) | 3 / 83 (3.61%) |
| occurrences (all) | 1 | 2 | 3 |
| Muscle atrophy | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Muscle spasms | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 1 / 42 (2.38%) | 0 / 83 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Muscle contracture | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 6 / 20 (30.00%) | 17 / 42 (40.48%) | 37 / 83 (44.58%) |
| occurrences (all) | 19 | 38 | 67 |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 1 / 42 (2.38%) | 0 / 83 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Limb asymmetry | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Musculoskeletal stiffness | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 42 (2.38%) | 1 / 83 (1.20%) |
| occurrences (all) | 0 | 1 | 1 |
| Pain in extremity | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 4 / 42 (9.52%) | 6 / 83 (7.23%) |
| occurrences (all) | 1 | 6 | 6 |
| Pathological fracture | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Scoliosis | | | |
| subjects affected / exposed | 6 / 20 (30.00%) | 22 / 42 (52.38%) | 33 / 83 (39.76%) |
| occurrences (all) | 7 | 32 | 48 |
| Spinal deformity | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Neck pain | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 42 (2.38%) | 1 / 83 (1.20%) |
| occurrences (all) | 0 | 1 | 1 |
| Neuromuscular scoliosis | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 42 (0.00%) | 1 / 83 (1.20%) |
| occurrences (all) | 2 | 0 | 1 |
| Osteopenia | | | |
| subjects affected / exposed | 2 / 20 (10.00%) | 1 / 42 (2.38%) | 3 / 83 (3.61%) |
| occurrences (all) | 2 | 1 | 3 |
| Osteoporosis | | | |
| subjects affected / exposed | 2 / 20 (10.00%) | 2 / 42 (4.76%) | 0 / 83 (0.00%) |
| occurrences (all) | 2 | 2 | 0 |
| Tendinous contracture | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 42 (2.38%) | 2 / 83 (2.41%) |
| occurrences (all) | 0 | 1 | 2 |
| Infections and infestations | | | |
| Abdominal abscess | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Bronchiolitis | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Adenovirus infection | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 42 (2.38%) | 2 / 83 (2.41%) |
| occurrences (all) | 0 | 1 | 2 |
| Bacterial disease carrier | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 1 / 83 (1.20%) |
| occurrences (all) | 0 | 0 | 2 |
| Bacterial infection | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 1 / 42 (2.38%) | 0 / 83 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Acute sinusitis | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 42 (0.00%) | 1 / 83 (1.20%) |
| occurrences (all) | 1 | 0 | 1 |
| Coronavirus infection | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Covid-19 | | | |
| subjects affected / exposed | 4 / 20 (20.00%) | 8 / 42 (19.05%) | 16 / 83 (19.28%) |
| occurrences (all) | 4 | 8 | 19 |
| Coxsackie viral infection | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Conjunctivitis | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 42 (2.38%) | 4 / 83 (4.82%) |
| occurrences (all) | 0 | 1 | 4 |
| Bronchitis | | | |
| subjects affected / exposed | 2 / 20 (10.00%) | 7 / 42 (16.67%) | 5 / 83 (6.02%) |
| occurrences (all) | 4 | 9 | 5 |

| | | | |
|---|---|---|---|
| Cellulitis | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Clostridium difficile infection | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Croup infectious | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cystitis | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 42 (2.38%) | 3 / 83 (3.61%) |
| occurrences (all) | 0 | 1 | 3 |
| Ear infection | | | |
| subjects affected / exposed | 3 / 20 (15.00%) | 5 / 42 (11.90%) | 14 / 83 (16.87%) |
| occurrences (all) | 3 | 6 | 19 |
| Ear infection fungal | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Enterovirus infection | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 42 (2.38%) | 2 / 83 (2.41%) |
| occurrences (all) | 0 | 1 | 2 |
| Gastroenteritis viral | | | |
| subjects affected / exposed | 7 / 20 (35.00%) | 5 / 42 (11.90%) | 3 / 83 (3.61%) |
| occurrences (all) | 7 | 5 | 7 |
| Fungal skin infection | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 1 / 42 (2.38%) | 0 / 83 (0.00%) |
| occurrences (all) | 3 | 1 | 0 |
| Gastritis viral | | | |
| subjects affected / exposed | 2 / 20 (10.00%) | 1 / 42 (2.38%) | 0 / 83 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 3 / 20 (15.00%) | 4 / 42 (9.52%) | 11 / 83 (13.25%) |
| occurrences (all) | 3 | 10 | 15 |
| Eye infection | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Gastrointestinal viral infection | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 42 (2.38%) | 1 / 83 (1.20%) |
| occurrences (all) | 0 | 1 | 1 |
| Hand-foot-and-mouth disease | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 42 (2.38%) | 3 / 83 (3.61%) |
| occurrences (all) | 0 | 1 | 3 |
| Hordeolum | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 42 (2.38%) | 2 / 83 (2.41%) |
| occurrences (all) | 0 | 1 | 3 |
| Impetigo | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 1 / 42 (2.38%) | 1 / 83 (1.20%) |
| occurrences (all) | 1 | 1 | 2 |
| Influenza | | | |
| subjects affected / exposed | 4 / 20 (20.00%) | 6 / 42 (14.29%) | 16 / 83 (19.28%) |
| occurrences (all) | 4 | 11 | 20 |
| Klebsiella infection | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 3 / 83 (3.61%) |
| occurrences (all) | 0 | 0 | 4 |
| Lower respiratory tract infection viral | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Metapneumovirus infection | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Otitis externa | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 3 / 83 (3.61%) |
| occurrences (all) | 0 | 0 | 3 |
| Oral fungal infection | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Otitis media | | | |
| subjects affected / exposed | 4 / 20 (20.00%) | 5 / 42 (11.90%) | 6 / 83 (7.23%) |
| occurrences (all) | 4 | 10 | 8 |

| | | | |
|---|---|---|---|
| Otitis media acute | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 2 / 42 (4.76%) | 2 / 83 (2.41%) |
| occurrences (all) | 0 | 2 | 2 |
| Moraxella infection | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Mycoplasma infection | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 4 / 20 (20.00%) | 13 / 42 (30.95%) | 27 / 83 (32.53%) |
| occurrences (all) | 7 | 37 | 72 |
| Oral candidiasis | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 42 (2.38%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 6 / 42 (14.29%) | 11 / 83 (13.25%) |
| occurrences (all) | 1 | 6 | 21 |
| Pharyngitis streptococcal | | | |
| subjects affected / exposed | 3 / 20 (15.00%) | 4 / 42 (9.52%) | 8 / 83 (9.64%) |
| occurrences (all) | 4 | 6 | 16 |
| Pseudomonas infection | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Parainfluenzae virus infection | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pharyngitis | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 4 / 42 (9.52%) | 3 / 83 (3.61%) |
| occurrences (all) | 1 | 5 | 3 |
| Pneumonia bacterial | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 1 / 83 (1.20%) |
| occurrences (all) | 0 | 0 | 1 |
| Postoperative wound infection | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 42 (2.38%) | 1 / 83 (1.20%) |
| occurrences (all) | 0 | 2 | 1 |

| | | | |
|---|---|---|---|
| Respiratory syncytial virus infection | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 2 / 42 (4.76%) | 1 / 83 (1.20%) |
| occurrences (all) | 0 | 2 | 1 |
| Pneumonia aspiration | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory tract infection | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 3 / 42 (7.14%) | 8 / 83 (9.64%) |
| occurrences (all) | 0 | 9 | 10 |
| Respiratory tract infection viral | | | |
| subjects affected / exposed | 2 / 20 (10.00%) | 1 / 42 (2.38%) | 2 / 83 (2.41%) |
| occurrences (all) | 3 | 1 | 2 |
| Rhinitis | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 3 / 42 (7.14%) | 8 / 83 (9.64%) |
| occurrences (all) | 0 | 4 | 16 |
| Rhinovirus infection | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 3 / 42 (7.14%) | 3 / 83 (3.61%) |
| occurrences (all) | 1 | 3 | 4 |
| Serratia infection | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sinusitis | | | |
| subjects affected / exposed | 2 / 20 (10.00%) | 3 / 42 (7.14%) | 6 / 83 (7.23%) |
| occurrences (all) | 2 | 3 | 13 |
| Staphylococcal infection | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Stenotrophomonas infection | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory tract infection bacterial | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Stoma site infection | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Suspected covid-19 | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Tonsillitis | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 3 / 42 (7.14%) | 6 / 83 (7.23%) |
| occurrences (all) | 0 | 3 | 6 |
| Tooth abscess | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Stoma site cellulitis | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 8 / 20 (40.00%) | 21 / 42 (50.00%) | 33 / 83 (39.76%) |
| occurrences (all) | 14 | 56 | 63 |
| Upper respiratory tract infection bacterial | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urinary tract infection | | | |
| subjects affected / exposed | 2 / 20 (10.00%) | 4 / 42 (9.52%) | 7 / 83 (8.43%) |
| occurrences (all) | 3 | 8 | 12 |
| Tracheitis | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 3 / 20 (15.00%) | 4 / 42 (9.52%) | 4 / 83 (4.82%) |
| occurrences (all) | 4 | 5 | 5 |
| Viral infection | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 2 / 42 (4.76%) | 10 / 83 (12.05%) |
| occurrences (all) | 0 | 7 | 11 |
| Metabolism and nutrition disorders | | | |
| Feeding intolerance | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 1 / 83 (1.20%) |
| occurrences (all) | 0 | 0 | 1 |
| Electrolyte imbalance | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 1 / 83 (1.20%) |
| occurrences (all) | 0 | 0 | 1 |
| Dehydration | | | |
| subjects affected / exposed | 1 / 20 (5.00%) | 4 / 42 (9.52%) | 2 / 83 (2.41%) |
| occurrences (all) | 1 | 4 | 2 |
| Hypocalcaemia | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 1 / 83 (1.20%) |
| occurrences (all) | 0 | 0 | 1 |
| Hyponatraemia | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 1 / 83 (1.20%) |
| occurrences (all) | 0 | 0 | 1 |
| Hypokalaemia | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 42 (2.38%) | 2 / 83 (2.41%) |
| occurrences (all) | 0 | 1 | 3 |
| Hypoglycaemia | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 42 (2.38%) | 1 / 83 (1.20%) |
| occurrences (all) | 0 | 2 | 1 |
| Hypochloraemia | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Malnutrition | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 4 / 83 (4.82%) |
| occurrences (all) | 0 | 0 | 4 |
| Iron deficiency | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypovolaemia | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Metabolic acidosis | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 2 / 42 (4.76%) | 2 / 83 (2.41%) |
| occurrences (all) | 0 | 2 | 2 |
| Obesity | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 2 / 42 (4.76%) | 4 / 83 (4.82%) |
| occurrences (all) | 0 | 2 | 4 |
| Vitamin d deficiency | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 42 (2.38%) | 1 / 83 (1.20%) |
| occurrences (all) | 0 | 1 | 1 |
| Weight gain poor | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 2 / 83 (2.41%) |
| occurrences (all) | 0 | 0 | 2 |
| Metabolic alkalosis | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 42 (0.00%) | 0 / 83 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 01 November 2015 | Allowed inclusion of participants who completed Study CS12 into Study CS11, and to provide clarifications and corrections to the original CS11 study protocol dated 12 May 2015. |
| 30 January 2017 | Transitioned the dosing regimen for the open-label maintenance dosing period for all index studies (ISIS 396443-CS3B [Groups 1A and 1B], ISIS 396443-CS4 [Groups 2A and 2B], ISIS 396443-CS12 [Group 3], and ISIS 396443-CS3A [Group 4]) to the MMDR schedule, during which maintenance doses of nusinersen were administered every 4 months. |
| 29 October 2017 | Allowed enrollment of participants from the newly added index study 232SM202 into this extension study. As a result of this change, the approximate number of participants had increased from 239 to 292 participants, the approximate number of study sites from 37 up to 45 sites, and the approximate number of countries from 14 up to 15 worldwide. Participants entering the extension study from the index study 232SM202 were enrolled into a new cohort, Group 5. Participants entered directly into the open-label period at MMDR Day 1. |
| 18 November 2019 | Changed the interval of clinical assessment visits after the Modified Maintenance Dosing Regimen (MMDR) Day 720 Visit from every 8 months to every 12 months. |
| 23 March 2020 | Changed the standard neurological examination to a focused neurological examination. |
| 20 October 2021 | Limited the number of participants who were receiving nusinersen concomitantly with other SMA therapies to 20% (n = 58) of the total population. |

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

None reported