# Clinical trial results:
# A Pivotal Phase 3 Study of MEDI-524 (Numax; Motavizumab), an Enhanced Potency Humanized Respiratory Syncytial Virus (RSV) Monoclonal Antibody, for the Prophylaxis of Serious RSV Disease in High-Risk Children

## Summary

| | |
|---|---|
| EudraCT number | 2004-000039-27 |
| Trial protocol | SE HU CZ DK IS AT IT GB |
| Global end of trial date | 08 May 2006 |

### Results information

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 10 February 2016 |
| First version publication date | 10 February 2016 |

## Trial information

### Trial identification

| | |
|---|---|
| Sponsor protocol code | MI-CP110 |

### Additional study identifiers

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00129766 |
| WHO universal trial number (UTN) | - |

Notes:

### Sponsors

| | |
|---|---|
| Sponsor organisation name | MedImmune, Inc. |
| Sponsor organisation address | One MedImmune Way, Gaithersburg, United States, MD 20878 |
| Public contact | M. Pamela Griffin, Sr. Director, Clinical Development, MedImmune, Inc., clinicaltrialenquiries@medimmune.com |
| Scientific contact | M. Pamela Griffin, Sr. Director, Clinical Development, MedImmune. Inc., clinicaltrialenquiries@medimmune.com |

Notes:

### Paediatric regulatory details

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

Notes:

## Results analysis stage

| | |
|---|---|
| Analysis stage | Final |
| Date of interim/final analysis | 08 May 2006 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 08 May 2006 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

The primary objective of this study was to compare the safety and efficacy of motavizumab to palivizumab when administered monthly by intramuscular (IM) injection for the reduction of the incidence of respiratory syncytial virus (RSV) hospitalization among children at high risk for serious RSV disease.

Protection of trial subjects:

The conduct of this clinical study met all local legal and regulatory requirements. The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and the International Conference on Harmonization guideline E6: Good Clinical Practice. Participating participant signed informed consent form and could withdraw from the study at any time without any disadvantage and without having to provide a reason for this decision. Only investigators qualified by training and experience were selected as appropriate experts to investigate the study drug.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 01 November 2004 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Safety |
| Long term follow-up duration | 5 Months |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | United States: 2297 |
| Country: Number of subjects enrolled | Greece: 66 |
| Country: Number of subjects enrolled | Spain: 372 |
| Country: Number of subjects enrolled | Turkey: 78 |
| Country: Number of subjects enrolled | Austria: 69 |
| Country: Number of subjects enrolled | Russian Federation: 87 |
| Country: Number of subjects enrolled | Israel: 606 |
| Country: Number of subjects enrolled | Chile: 180 |
| Country: Number of subjects enrolled | United Kingdom: 179 |
| Country: Number of subjects enrolled | Italy: 189 |
| Country: Number of subjects enrolled | France: 218 |
| Country: Number of subjects enrolled | Hungary: 390 |
| Country: Number of subjects enrolled | Czech Republic: 348 |
| Country: Number of subjects enrolled | Canada: 266 |
| Country: Number of subjects enrolled | Argentina: 72 |

| | |
|---|---|
| Country: Number of subjects enrolled | Poland: 211 |
| Country: Number of subjects enrolled | Brazil: 135 |
| Country: Number of subjects enrolled | Australia: 166 |
| Country: Number of subjects enrolled | Denmark: 57 |
| Country: Number of subjects enrolled | Bulgaria: 196 |
| Country: Number of subjects enrolled | Iceland: 39 |
| Country: Number of subjects enrolled | Germany: 253 |
| Country: Number of subjects enrolled | New Zealand: 52 |
| Country: Number of subjects enrolled | Sweden: 109 |
| Worldwide total number of subjects | 6635 |
| EEA total number of subjects | 2696 |

Notes:

**Subjects enrolled per age group**

| | |
|---|---|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 779 |
| Infants and toddlers (28 days-23 months) | 5838 |
| Children (2-11 years) | 18 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

A total of 6,635 children were randomized in a 1:1 ratio at 347 centers in 24 countries within the Northern and Southern hemispheres between 01/Nov/2004 and 09/Dec/2005; each child participated in the study for a single respiratory syncytial virus (RSV) season.

### Pre-assignment

Screening details:

Randomization was blocked by study site and stratified according to presence/absence of chronic lung disease (CLD) of prematurity requiring medical intervention/management.

### Period 1

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

### Arms

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

Arm description:

Palivizumab, 15 mg/kg administered intramuscularly for 5 monthly doses

| | |
|---|---|
| Arm type | Active comparator |
| Investigational medicinal product name | Palivizumab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Palivizumab, 15 mg/kg administered intramuscularly for 5 monthly doses

| | |
|---|---|
| **Arm title** | Motavizumab |

Arm description:

Motavizumab, 15 mg/kg administered intramuscularly for 5 monthly doses

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Motavizumab |
| Investigational medicinal product code | MEDI-524 |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Motavizumab, 15 mg/kg administered intramuscularly for 5 monthly doses

| **Number of subjects in period 1** | Palivizumab | Motavizumab |
|---|---|---|
| Started | 3306 | 3329 |
| Completed | 3246 | 3270 |
| Not completed | 60 | 59 |
| Adverse event, serious fatal | 3 | 8 |
| Withdrawal of consent | 31 | 30 |
| Lost to follow-up | 26 | 21 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Palivizumab |
| Reporting group description: | |
| Palivizumab, 15 mg/kg administered intramuscularly for 5 monthly doses | |
| Reporting group title | Motavizumab |
| Reporting group description: | |
| Motavizumab, 15 mg/kg administered intramuscularly for 5 monthly doses | |

| Reporting group values | Palivizumab | Motavizumab | Total |
|---|---|---|---|
| Number of subjects | 3306 | 3329 | 6635 |
| Age categorical<br>Units: Subjects | | | |
| Age Continuous \|<br>Units: months | | | |
| arithmetic mean | 3.98 | 3.99 | |
| standard deviation | ± 3.78 | ± 3.75 | - |
| Gender, Male/Female<br>Units: participants | | | |
| Female | 1495 | 1513 | 3008 |
| Male | 1811 | 1816 | 3627 |
| Region of Enrollment<br>Units: Subjects | | | |
| United States | 1130 | 1167 | 2297 |
| Greece | 32 | 34 | 66 |
| Spain | 191 | 181 | 372 |
| Turkey | 36 | 42 | 78 |
| Austria | 35 | 34 | 69 |
| Russian Federation | 42 | 45 | 87 |
| Israel | 301 | 305 | 606 |
| Chile | 93 | 87 | 180 |
| United Kingdom | 89 | 90 | 179 |
| Italy | 93 | 96 | 189 |
| France | 107 | 111 | 218 |
| Hungary | 198 | 192 | 390 |
| Czech Republic | 171 | 177 | 348 |
| Canada | 134 | 132 | 266 |
| Argentina | 38 | 34 | 72 |
| Poland | 106 | 105 | 211 |
| Brazil | 69 | 66 | 135 |
| Australia | 85 | 81 | 166 |
| Denmark | 30 | 27 | 57 |
| Bulgaria | 95 | 101 | 196 |
| Iceland | 20 | 19 | 39 |
| Germany | 131 | 122 | 253 |
| New Zealand | 26 | 26 | 52 |
| Sweden | 54 | 55 | 109 |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Palivizumab |
| Reporting group description: | |
| Palivizumab, 15 mg/kg administered intramuscularly for 5 monthly doses | |
| Reporting group title | Motavizumab |
| Reporting group description: | |
| Motavizumab, 15 mg/kg administered intramuscularly for 5 monthly doses | |

### Primary: Incidence of Respiratory Syncytial Virus (RSV) Hospitalization (Includes Deaths by RSV)

| | |
|---|---|
| End point title | Incidence of Respiratory Syncytial Virus (RSV) Hospitalization (Includes Deaths by RSV) |
| End point description: | |
| RSV hospitalization was defined as 1) a respiratory hospitalization with a positive RSV test (primary), 2) a new onset of lower respiratory symptoms in an already hospitalized child, with an objective measure of worsening respiratory status and positive RSV test (nosocomial), or 3) death demonstrated to have been caused by RSV (by autopsy or clinical history and virologic evidence). The Intent-to-Treat (ITT) Population included all patients randomized into the study. | |
| End point type | Primary |
| End point timeframe: | |
| Days 0 - 150 | |

| End point values | Palivizumab | Motavizumab | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 3306 | 3329 | | |
| Units: Participants | 62 | 46 | | |

### Statistical analyses

| Statistical analysis title | Statistical analysis 1 |
|---|---|
| Statistical analysis description: | |
| ITT population. Relative risk was calculated as (Pn/Ps) where Pn is the proportion of patients with RSV hospitalization in the motavizumab group and Ps is the proportion of patients with RSV hospitalization in the palivizumab group. | |
| Comparison groups | Palivizumab v Motavizumab |
| Number of subjects included in analysis | 6635 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[1] |
| Method | t-test, 2-sided |
| Parameter estimate | Risk ratio (RR) |
| Point estimate | 0.74 |

| Confidence interval | |
|---|---|
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.503 |
| upper limit | 1.083 |

Notes:

[1] - Confidence interval and relative risk adjusted for the stratification factor of presence or absence of CLD of prematurity as specified on the CRF.

## Primary: Number of Participants Reporting any Adverse Events (AEs)

| End point title | Number of Participants Reporting any Adverse Events (AEs)[2] |
|---|---|

End point description:

Number of participants reporting one or more AEs. The Safety Population included all patients who received any study drug and had any safety follow-up.

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

End point timeframe:

Days 0 - 150

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: Descriptive statistics were done, no inferential statistical analyses were performed.

| End point values | Palivizumab | Motavizumab | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 3298 | 3315 | | |
| Units: Participants | 2837 | 2839 | | |

### Statistical analyses

No statistical analyses for this end point

## Primary: Number of Participants Reporting Any Related AEs

| End point title | Number of Participants Reporting Any Related AEs[3] |
|---|---|

End point description:

Number of participants reporting one or more AEs considered related to study drug by the investigator. The Safety Population included all patients who received any study drug and had any safety follow-up.

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

End point timeframe:

Days 0 - 150

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: Descriptive statistics were done, no inferential statistical analyses were performed.

| End point values | Palivizumab | Motavizumab | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 3298 | 3315 | | |
| Units: Participants | 258 | 298 | | |

## Statistical analyses

No statistical analyses for this end point

## Primary: Number of Participants Reporting any Serious Adverse Events (SAEs)

| End point title | Number of Participants Reporting any Serious Adverse Events (SAEs)[4] |
|---|---|

End point description:

Number of participants reporting one or more SAEs. The Safety Population included all patients who received any study drug and had any safety follow-up.

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

End point timeframe:

Days 0 - 150

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: Descriptive statistics were done, no inferential statistical analyses were performed.

| **End point values** | Palivizumab | Motavizumab | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 3298 | 3315 | | |
| Units: Participants | 506 | 485 | | |

## Statistical analyses

No statistical analyses for this end point

## Primary: Number of Participants Reporting any Related SAEs

| End point title | Number of Participants Reporting any Related SAEs[5] |
|---|---|

End point description:

Number of participants reporting one or more SAEs considered related to study drug by the investigator. The Safety Population included all patients who received any study drug and had any safety follow-up.

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

End point timeframe:

Days 0 - 150

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: Descriptive statistics were done, no inferential statistical analyses were performed.

| End point values | Palivizumab | Motavizumab | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 3298 | 3315 | | |
| Units: Participants | 8 | 9 | | |

### Statistical analyses

No statistical analyses for this end point

### Primary: Number of Participants Reporting AEs by Highest Severity Grade

| End point title | Number of Participants Reporting AEs by Highest Severity Grade[6] |
|---|---|

End point description:

Adverse events events were graded by severity; Level 1, 2, 3, or 4. The Safety Population included all patients who received any study drug and had any safety follow-up.

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

End point timeframe:

Days 0 - 150

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: Descriptive statistics were done, no inferential statistical analyses were performed.

| End point values | Palivizumab | Motavizumab | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 3298 | 3315 | | |
| Units: Participants | | | | |
| Level 1 | 1478 | 1538 | | |
| Level 2 | 1006 | 976 | | |
| Level 3 | 292 | 271 | | |
| Level 4 | 61 | 54 | | |

### Statistical analyses

No statistical analyses for this end point

### Primary: Number of Participants who Discontinued Study Drug due to AEs

| End point title | Number of Participants who Discontinued Study Drug due to AEs[7] |
|---|---|

End point description:

The Safety Population included all patients who received any study drug and had any safety follow-up.

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

End point timeframe:

Days 0 - 150

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: Descriptive statistics were done, no inferential statistical analyses were performed.

| End point values | Palivizumab | Motavizumab | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 3298 | 3315 | | |
| Units: Participants | 10 | 13 | | |

### Statistical analyses

No statistical analyses for this end point

### Primary: Number of Participants who Died

| End point title | Number of Participants who Died[8] |
|---|---|

End point description:

The Safety Population included all patients who received any study drug and had any safety follow-up.

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

End point timeframe:

Days 0 - 150

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: Descriptive statistics were done, no inferential statistical analyses were performed.

| End point values | Palivizumab | Motavizumab | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 3298 | 3315 | | |
| Units: Participants | 4 | 8 | | |

### Statistical analyses

No statistical analyses for this end point

### Primary: Number of Participants Reporting Changes in Vital Signs From Baseline

| End point title | Number of Participants Reporting Changes in Vital Signs From Baseline[9] |
|---|---|

End point description:

Vital signs that were in a higher toxicity grade than observed at baseline were to be recorded as AEs.
The Safety Population included all patients who received any study drug and had any safety follow-up.

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

End point timeframe:

Days 0 - 150

Notes:

[9] - 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: Descriptive statistics were done, no inferential statistical analyses were performed.

| **End point values** | Palivizumab | Motavizumab | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 3298 | 3315 | | |
| Units: Participants | | | | |
| Fever neonatal | 0 | 2 | | |
| Hyperpyrexia | 0 | 1 | | |
| Hyperthermia | 3 | 3 | | |
| Hypothermia | 2 | 2 | | |
| Pyrexia | 559 | 544 | | |
| Hypertension | 4 | 4 | | |
| Hypotension | 2 | 2 | | |
| Arrhythmia | 1 | 0 | | |
| Bradycardia | 10 | 4 | | |
| Tachycardia | 4 | 6 | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: The Incidence of Outpatient Medically-Attended Lower Respiratory Illness (LRI)

| End point title | The Incidence of Outpatient Medically-Attended Lower Respiratory Illness (LRI) |
|---|---|

End point description:

LRI was defined as an event of bronchiolitis or pneumonia or the occurance of a lower tract infectious illness as determined by the PI based on medical history, signs, and symptoms. The Intent-to-Treat (ITT) Population included all patients randomized into the study.

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

End point timeframe:

Day 0 - 150

| **End point values** | Palivizumab | Motavizumab | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 3306 | 3329 | | |
| Units: Participant | 696 | 648 | | |

## Statistical analyses

| **Statistical analysis title** | Statistical analysis 1 |
|---|---|
| Comparison groups | Palivizumab v Motavizumab |

| | |
|---|---|
| Number of subjects included in analysis | 6635 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[10] |
| P-value | = 0.11 [11] |
| Method | Van Elteren test |

Notes:

[10] - A Van Elteren test stratified for presence or absence of CLD of prematurity requiring medical intervention was used.
[11] - Test stratified by presence or absence of CLD of prematurity specified on the CRF

## Secondary: The Incidence of RSV-Specific Medically-Attended Outpatient Lower Respiratory Illnesses (LRIs) Between Treatment Groups

| | |
|---|---|
| End point title | The Incidence of RSV-Specific Medically-Attended Outpatient Lower Respiratory Illnesses (LRIs) Between Treatment Groups |

End point description:

The RSV-specific LRI was defined as an outpatient medically-attended LRI associated with a positive RSV test and was not inclusive of events that required hospitalization. Participants were from a pre-specified subsets of sites participating in the nasal secretion sample collection for this endpoint.

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

End point timeframe:

Days 0 - 150

| End point values | Palivizumab | Motavizumab | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1183 | 1227 | | |
| Units: Participants | 46 | 24 | | |

### Statistical analyses

| Statistical analysis title | Statistical analysis 1 |
|---|---|
| Comparison groups | Palivizumab v Motavizumab |
| Number of subjects included in analysis | 2410 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[12] |
| P-value | = 0.005 [13] |
| Method | Van Elteren test |

Notes:

[12] - A Van Elteren test stratified for presence or absence of CLD of prematurity requiring medical intervention was used.
[13] - No adjustment for multiple comparisons.

## Secondary: The Overall Incidence of Medically-Attended Otitis Media (OM) Infections

| | |
|---|---|
| End point title | The Overall Incidence of Medically-Attended Otitis Media (OM) Infections |

End point description:

Otitis media (OM) was to be recorded as the diagnosis if the following terms were used by the medical care provider: acute OM, acute tympanic membrane (TM) perforation, bulging TM, red TM with fever, OM with effusion, or middle ear effusion. A new episode was defined as a physician-diagnosed OM in either ear after a normal middle ear exam of the ear in question or an episode of acute OM greater than

or equal to 21 days after resolution of the previous episode. A diagnosis of persistent middle ear effusion was not to be recorded as a new OM event. The ITT population included all patients randomized into the study.

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

End point timeframe:

Days 0 - 150

| **End point values** | Palivizumab | Motavizumab | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 3306 | 3329 | | |
| Units: Participants | 461 | 484 | | |

## Statistical analyses

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

Statistical analysis description:

P-value is for overall incidence

| Comparison groups | Palivizumab v Motavizumab |
|---|---|
| Number of subjects included in analysis | 6635 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[14] |
| P-value | = 0.476 [15] |
| Method | Van Elteren test |

Notes:

[14] - A Van Elteren test stratified for presence or absence of CLD of prematurity requiring medical intervention was used.
[15] - Test stratified by presence or absence of CLD of prematurity specified on the CRF

## Secondary: The Frequency of Prescribed Antibiotics for Medically-Attended LRI

| End point title | The Frequency of Prescribed Antibiotics for Medically-Attended LRI |
|---|---|

End point description:

The average number of presciptions per event per subject was summarized for each treatment group. The ITT population included all patients randomized into the study.

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

End point timeframe:

Days 0 - 150

| **End point values** | Palivizumab | Motavizumab | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 3306 | 3329 | | |
| Units: Number of prescriptions | | | | |
| arithmetic mean (standard error) | 0.32 (± 0.02) | 0.3 (± 0.02) | | |

### Statistical analyses

| Statistical analysis title | Statistical analysis 1 |
|---|---|
| Comparison groups | Palivizumab v Motavizumab |
| Number of subjects included in analysis | 6635 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[16] |
| P-value | = 0.493 [17] |
| Method | Van Elteren test |

Notes:

[16] - A Van Elteren test stratified for presence or absence of CLD of prematurity requiring medical intervention was used.
[17] - Test stratified by presence or absence of CLD of prematurity specified on the CRF

## Secondary: The Frequency of Prescribed Antibiotics for Medically-Attended OM Infections

| End point title | The Frequency of Prescribed Antibiotics for Medically-Attended OM Infections |
|---|---|

End point description:

The average number of presciptions per event per subject was summarized for each treatment group. The ITT population included all patients randomized into the study.

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

End point timeframe:

Days 0 - 150

| End point values | Palivizumab | Motavizumab | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 3306 | 3329 | | |
| Units: Number of prescriptions | | | | |
| arithmetic mean (standard error) | 1.08 (± 0.003) | 1.1 (± 0.003) | | |

### Statistical analyses

| Statistical analysis title | Statistical analysis 1 |
|---|---|
| Comparison groups | Palivizumab v Motavizumab |

| | |
|---|---|
| Number of subjects included in analysis | 6635 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[18] |
| P-value | = 0.652 [19] |
| Method | Van Elteren test |

Notes:

[18] - A Van Elteren test stratified for presence or absence of CLD of prematurity requiring medical intervention was used.
[19] - Test stratified by presence or absence of CLD of prematurity specified on the CRF

## Secondary: The Number of Participants With Anti-Motavizumab Antibodies

| | |
|---|---|
| End point title | The Number of Participants With Anti-Motavizumab |

End point description:

Detection of anti-motavizumab antibodies was defined as a titer with a dilution value equal to or greater than 1:10. N varied at different timepoints: at pre-dose 1 N=3193; at 30 days post-dose 1 N=998; at 30 days post-dose 2 N=1049; at 30 days post-dose 3 N=1049; at 30 days post-dose 4, N=3013; at any time post baseline, N=3217

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

End point timeframe:

Day 0 - 120

Notes:

[20] - 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: Descriptive statistics were done, no inferential statistical analyses were performed.

| **End point values** | Motavizumab | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 3217 | | | |
| Units: Participants | | | | |
| Pre-dose 1 | 7 | | | |
| 30 Days Post-Dose 1 | 1 | | | |
| 30 Days Post-Dose 2 | 1 | | | |
| 30 Days Post-Dose 3 | 7 | | | |
| 30 Days Post-Dose 4 | 18 | | | |
| At any time post baseline | 22 | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: The Serum Concentrations of Motavizumab at Day 0

| | |
|---|---|
| End point title | The Serum Concentrations of Motavizumab at Day 0[21] |

End point description:

Mean serum concentrations of motavizumab at Day 0. The Pharmacokinetics/Immunogenicity (PK/IM) Population included all patients who received study drug and who did not receive non-study commercial palivizumab within 3 months prior to receiving the first dose of study drug.

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

End point timeframe:

Day 0

Notes:

[21] - 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: Descriptive statistics were done, no inferential statistical analyses were performed.

| **End point values** | Motavizumab | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 3147 | | | |
| Units: microgram per milliliter (mcg/mL) | | | | |
| arithmetic mean (standard deviation) | 0.01193 (± 0.2072) | | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: The Trough Serum Concentrations of Motavizumab at 30 days Post Dose 1

| End point title | The Trough Serum Concentrations of Motavizumab at 30 days Post Dose 1[22] |
|---|---|

End point description:

Mean serum concentrations of motavizumab at 30 days post Dose 1. The Pharmacokinetics/Immunogenicity (PK/IM) Population included all patients who received study drug and who did not receive non-study commercial palivizumab within 3 months prior to receiving the first dose of study drug. Includes subjects with both baseline and a post-dose 1 measurements

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

End point timeframe:

30 days post Dose 1

Notes:

[22] - 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: Descriptive statistics were done, no inferential statistical analyses were performed.

| **End point values** | Motavizumab | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 974 | | | |
| Units: mcg/mL | | | | |
| arithmetic mean (standard deviation) | 45.95 (± 15.17) | | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: The Trough Serum Concentrations of Motavizumab at 30 days Post Dose 3

| End point title | The Trough Serum Concentrations of Motavizumab at 30 days Post Dose 3[23] |
|---|---|

End point description:

Mean serum concentrations of motavizumab at 30 days post Dose 3. The Pharmacokinetics/Immunogenicity (PK/IM) Population included all patients who received study drug and who did not receive non-study commercial palivizumab within 3 months prior to receiving the first dose of study drug. Includes subjects with both baseline and a post-dose 3 measurements

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

End point timeframe:

30 days post Dose 3

Notes:

[23] - 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: Descriptive statistics were done, no inferential statistical analyses were performed.

| **End point values** | Motavizumab | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 918 | | | |
| Units: mcg/mL | | | | |
| arithmetic mean (standard deviation) | 80.24 (± 31.22) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: The Trough Serum Concentrations of Motavizumab at 30 days Post Dose 2

| End point title | The Trough Serum Concentrations of Motavizumab at 30 days Post Dose 2[24] |
|---|---|

End point description:

Mean serum concentrations of motavizumab at 30 days post Dose 2. The Pharmacokinetics/Immunogenicity (PK/IM) Population included all patients who received study drug and who did not receive non-study commercial palivizumab within 3 months prior to receiving the first dose of study drug. Includes subjects with both baseline and a post-dose 2 measurements

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

End point timeframe:

30 days post Dose 2

Notes:

[24] - 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: Descriptive statistics were done, no inferential statistical analyses were performed.

| **End point values** | Motavizumab | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 915 | | | |
| Units: mcg/mL | | | | |
| arithmetic mean (standard deviation) | 64.59 (± 25.6) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: The Frequency of Medically-Attended Otitis Media (OM) Infections

| End point title | The Frequency of Medically-Attended Otitis Media (OM) Infections |
|---|---|

End point description:

Otitis media (OM) was to be recorded as the diagnosis if the following terms were used by the medical care provider: acute OM, acute tympanic membrane (TM) perforation, bulging TM, red TM with fever, OM with effusion, or middle ear effusion. A new episode was defined as a physician-diagnosed OM in either ear after a normal middle ear exam of the ear in question or an episode of acute OM greater than or equal to 21 days after resolution of the previous episode. A diagnosis of persistent middle ear effusion was not to be recorded as a new OM event. The ITT population included all patients randomized into the study.

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

End point timeframe:

Days 0 – 150

| End point values | Palivizumab | Motavizumab | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 3306 | 3329 | | |
| Units: participants | | | | |
| 0 infections | 2845 | 2845 | | |
| 1 infection | 329 | 360 | | |
| 2 infections | 100 | 91 | | |
| 3 or more infections | 32 | 33 | | |

## Statistical analyses

| Statistical analysis title | Statistical analysis 1 |
|---|---|
| Comparison groups | Palivizumab v Motavizumab |
| Number of subjects included in analysis | 6635 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[25] |
| P-value | = 0.5 [26] |
| Method | Van Elteren test |

Notes:

[25] - A Van Elteren test stratified for presence or absence of CLD of prematurity requiring medical intervention was used.

[26] - Test stratified by presence or absence of CLD of prematurity specified on the CRF

## Secondary: The Trough Serum Concentrations of Motavizumab at 30 days Post Dose 4

| End point title | The Trough Serum Concentrations of Motavizumab at 30 days Post Dose 4[27] |
|---|---|

End point description:

Mean serum concentrations of motavizumab at 30 days post Dose 4. The Pharmacokinetics/Immunogenicity (PK/IM) Population included all patients who received study drug and who did not receive non-study commercial palivizumab within 3 months prior to receiving the first dose

of study drug. Includes subjects with both baseline and a post-dose 4 measurements

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

End point timeframe:

30 days post Dose 4

Notes:

[27] - 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: Descriptive statistics were done, no inferential statistical analyses were performed.

| **End point values** | Motavizumab | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 2669 | | | |
| Units: mcg/mL | | | | |
| arithmetic mean (standard deviation) | 88.52 (± 35.43) | | | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

| Adverse events information | |
|---|---|
| Timeframe for reporting adverse events: Day 0 - Day 150 | |
| Assessment type | Systematic |

| Dictionary used | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 11.1 |

| Reporting groups | |
|---|---|
| Reporting group title | Motavizumab |
| Reporting group description: Motavizumab, 15 mg/kg administered intramuscularly for 5 monthly doses | |
| Reporting group title | Palivizumab |
| Reporting group description: Palivizumab, 15 mg/kg administered intramuscularly for 5 monthly doses | |

| Serious adverse events | Motavizumab | Palivizumab | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 485 / 3315 (14.63%) | 506 / 3298 (15.34%) | |
| number of deaths (all causes) | 8 | 4 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| HAEMANGIOMA | | | |
| subjects affected / exposed | 4 / 3315 (0.12%) | 4 / 3298 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 7 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| HAEMORRHAGE | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| HYPERTENSION | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 2 / 3298 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Surgical and medical procedures | | | |

| | | | |
|---|---|---|---|
| CENTRAL VENOUS CATHETERISATION | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| COLOSTOMY CLOSURE | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| EAR TUBE INSERTION | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| GASTROSTOMY CLOSURE | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| GASTROSTOMY TUBE INSERTION | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| ILEOSTOMY CLOSURE | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 3 / 3298 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| NUTRITIONAL SUPPORT | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| VENTRICULO-PERITONEAL SHUNT | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |

| | | | |
|---|---|---|---|
| FEVER NEONATAL | | | |
| subjects affected / exposed | 2 / 3315 (0.06%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| HERNIA OBSTRUCTIVE | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| HERNIA | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| HYPOTHERMIA | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| OEDEMA PERIPHERAL | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| MALAISE | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| SUDDEN DEATH | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| PYREXIA | | | |
| subjects affected / exposed | 10 / 3315 (0.30%) | 9 / 3298 (0.27%) | |
| occurrences causally related to treatment / all | 2 / 11 | 0 / 9 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| SUDDEN INFANT DEATH SYNDROME | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 3 / 3315 (0.09%) | 2 / 3298 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 3 | 0 / 2 | |
| Immune system disorders | | | |
| DRUG HYPERSENSITIVITY | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| HYPERSENSITIVITY | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| IMMUNISATION REACTION | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Social circumstances | | | |
| SOCIAL STAY HOSPITALISATION | | | |
| subjects affected / exposed | 4 / 3315 (0.12%) | 2 / 3298 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| VICTIM OF CHILD ABUSE | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Reproductive system and breast disorders | | | |
| BALANITIS | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| OVARIAN CYST | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| SCROTAL OEDEMA | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| APNOEA | | | |
| subjects affected / exposed | 14 / 3315 (0.42%) | 17 / 3298 (0.52%) | |
| occurrences causally related to treatment / all | 0 / 16 | 0 / 23 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| APPARENT LIFE THREATENING EVENT | | | |
| subjects affected / exposed | 2 / 3315 (0.06%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| ASTHMA | | | |
| subjects affected / exposed | 7 / 3315 (0.21%) | 5 / 3298 (0.15%) | |
| occurrences causally related to treatment / all | 0 / 7 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| ASPIRATION | | | |
| subjects affected / exposed | 2 / 3315 (0.06%) | 2 / 3298 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| ATELECTASIS | | | |
| subjects affected / exposed | 2 / 3315 (0.06%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| BRONCHIAL HYPERREACTIVITY | | | |
| subjects affected / exposed | 7 / 3315 (0.21%) | 7 / 3298 (0.21%) | |
| occurrences causally related to treatment / all | 0 / 7 | 0 / 8 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| BRONCHOPNEUMOPATHY | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| BRONCHOPULMONARY DYSPLASIA | | | |
| subjects affected / exposed | 9 / 3315 (0.27%) | 10 / 3298 (0.30%) | |
| occurrences causally related to treatment / all | 0 / 11 | 0 / 10 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| BRONCHOSPASM | | | |
| subjects affected / exposed | 3 / 3315 (0.09%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| CHOKING | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 2 / 3298 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| COUGH | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| FOREIGN BODY ASPIRATION | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| HYPOVENTILATION | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| HYPOXIA | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 2 / 3298 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| INTERSTITIAL LUNG DISEASE | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| LARYNGEAL STENOSIS | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 3315 (0.03%) | 3 / 3298 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| LARYNGEAL OEDEMA | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| LARYNGOSPASM | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| LUNG CONSOLIDATION | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| NASAL CONGESTION | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| OBSTRUCTIVE AIRWAYS DISORDER | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 2 / 3298 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| PHARYNGEAL INFLAMMATION | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PNEUMONIA ASPIRATION | | | |
| subjects affected / exposed | 3 / 3315 (0.09%) | 2 / 3298 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PNEUMOTHORAX | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 3315 (0.06%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PULMONARY CONGESTION | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PULMONARY HAEMORRHAGE | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PULMONARY HYPERTENSION | | | |
| subjects affected / exposed | 2 / 3315 (0.06%) | 4 / 3298 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 7 | |
| deaths causally related to treatment / all | 0 / 2 | 0 / 0 | |
| PULMONARY HYPERTENSIVE CRISIS | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PULMONARY OEDEMA | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| RESPIRATORY DISORDER | | | |
| subjects affected / exposed | 2 / 3315 (0.06%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| RESPIRATORY DISTRESS | | | |
| subjects affected / exposed | 2 / 3315 (0.06%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| RESPIRATORY FAILURE | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| SLEEP APNOEA SYNDROME | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 2 / 3298 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| STATUS ASTHMATICUS | | | |
| subjects affected / exposed | 2 / 3315 (0.06%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| STRIDOR | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| TACHYPNOEA | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| TONSILLAR HYPERTROPHY | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| VOCAL CORD DISORDER | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| WHEEZING | | | |
| subjects affected / exposed | 5 / 3315 (0.15%) | 3 / 3298 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 7 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| BREATH HOLDING | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3315 (0.00%) | 2 / 3298 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| RESTLESSNESS | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Investigations | | | |
| BIOPSY RECTUM | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| BLOOD BILIRUBIN INCREASED | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| CYSTOGRAM | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| FALSE POSITIVE LABORATORY RESULT | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| HEPATIC ENZYME INCREASED | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| INVESTIGATION | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| LIVER FUNCTION TEST ABNORMAL | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3315 (0.00%) | 2 / 3298 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| MEDICAL OBSERVATION | | | |
| subjects affected / exposed | 2 / 3315 (0.06%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| NEUROLOGICAL EXAMINATION | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 2 / 3298 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| OESOPHAGEAL PH | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| OXYGEN SATURATION DECREASED | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 2 / 3298 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PHYSICAL EXAMINATION | | | |
| subjects affected / exposed | 3 / 3315 (0.09%) | 3 / 3298 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| WEIGHT DECREASED | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 2 / 3298 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| CHILD MALTREATMENT SYNDROME | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| DEVICE MALFUNCTION | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| FACE INJURY | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| FEEDING TUBE COMPLICATION | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| FOREIGN BODY TRAUMA | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| HAIR-THREAD TOURNIQUET SYNDROME | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| HEAD INJURY | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 3 / 3298 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| INJURY | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| MEDICAL DEVICE COMPLICATION | | | |
| subjects affected / exposed | 2 / 3315 (0.06%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| POST PROCEDURAL DISCHARGE | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| SHUNT MALFUNCTION | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| SKULL FRACTURE | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| SUBDURAL HAEMATOMA | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| TRAUMATIC BRAIN INJURY | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| VENTRICULOPERITONEAL SHUNT MALFUNCTION | | | |
| subjects affected / exposed | 2 / 3315 (0.06%) | 4 / 3298 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| VIIITH NERVE INJURY | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Congenital, familial and genetic disorders | | | |
| ACRODERMATITIS ENTEROPATHICA | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| ANAL ATRESIA | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| ANKYLOGLOSSIA CONGENITAL | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| BRANCHIAL CLEFT CYST | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| CEREBRAL PALSY | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| CLEFT LIP | | | |
| subjects affected / exposed | 2 / 3315 (0.06%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| CLEFT LIP AND PALATE | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| CLEFT PALATE | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 2 / 3298 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| DACRYOSTENOSIS CONGENITAL | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| DERMOID CYST | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| HAMARTOMA | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| HIP DYSPLASIA | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| LIMB REDUCTION DEFECT | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PHIMOSIS | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PILONIDAL CYST CONGENITAL | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PYLORIC STENOSIS | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| RESPIRATORY TRACT MALFORMATION | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| SYNDACTYLY | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| TALIPES | | | |
| subjects affected / exposed | 2 / 3315 (0.06%) | 2 / 3298 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 7 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| TRACHEO-OESOPHAGEAL FISTULA | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| VENTRICULAR SEPTAL DEFECT | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| ATRIAL THROMBOSIS | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| BRADYCARDIA | | | |
| subjects affected / exposed | 2 / 3315 (0.06%) | 4 / 3298 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| CARDIAC ARREST | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| CARDIAC FAILURE HIGH OUTPUT | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| CARDIO-RESPIRATORY ARREST | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| CARDIOGENIC SHOCK | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| CYANOSIS | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 2 / 3298 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| SUPRAVENTRICULAR TACHYCARDIA | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| TACHYCARDIA | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| ALTERED STATE OF CONSCIOUSNESS | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| CEREBRAL VENTRICLE DILATATION | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| CONVULSION | | | |
| subjects affected / exposed | 3 / 3315 (0.09%) | 4 / 3298 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| CONVULSION NEONATAL | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| ENCEPHALITIS | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| FEBRILE CONVULSION | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| EPILEPSY | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| HAEMORRHAGE INTRACRANIAL | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| HYDROCEPHALUS | | | |
| subjects affected / exposed | 5 / 3315 (0.15%) | 2 / 3298 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| HYPERTONIA | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| HYPOXIC ENCEPHALOPATHY | | | |
| subjects affected / exposed | 4 / 3315 (0.12%) | 3 / 3298 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| INTRACRANIAL PRESSURE INCREASED | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| MYOCLONUS | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| LETHARGY | | | |
| subjects affected / exposed | 2 / 3315 (0.06%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| SOMNOLENCE | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| SYNCOPE VASOVAGAL | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| VOCAL CORD PARESIS | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| ANAEMIA | | | |
| subjects affected / exposed | 5 / 3315 (0.15%) | 4 / 3298 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| ANAEMIA NEONATAL | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 3 / 3298 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| CYCLIC NEUTROPENIA | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| HAEMOLYTIC ANAEMIA | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| HAEMOLYTIC URAEMIC SYNDROME | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| IRON DEFICIENCY ANAEMIA | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| NEUTROPENIA | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 2 / 3298 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| THROMBOCYTOPENIA | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ear and labyrinth disorders | | | |
| DEAFNESS | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Eye disorders | | | |
| PAPILLOEDEMA | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| RETINOPATHY OF PREMATURITY | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 5 / 3315 (0.15%) | 7 / 3298 (0.21%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 7 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| RETINOPATHY PROLIFERATIVE | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| ABDOMINAL DISTENSION | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| ABDOMINAL PAIN | | | |
| subjects affected / exposed | 2 / 3315 (0.06%) | 3 / 3298 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| ABDOMINAL STRANGULATED HERNIA | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| ANAL FISTULA | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| CONSTIPATION | | | |
| subjects affected / exposed | 2 / 3315 (0.06%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| COLONIC STENOSIS | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| DIARRHOEA | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 3315 (0.06%) | 5 / 3298 (0.15%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| DYSPEPSIA | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| DYSPHAGIA | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| ENTERITIS | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| ENTEROCOLITIS | | | |
| subjects affected / exposed | 2 / 3315 (0.06%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| FAECES DISCOLOURED | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| ENTEROCUTANEOUS FISTULA | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| FLATULENCE | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 2 / 3298 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| GASTROINTESTINAL HAEMORRHAGE | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| GASTROINTESTINAL DISORDER | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| HIATUS HERNIA | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| GASTROOESOPHAGEAL REFLUX DISEASE | | | |
| subjects affected / exposed | 18 / 3315 (0.54%) | 21 / 3298 (0.64%) | |
| occurrences causally related to treatment / all | 0 / 20 | 0 / 22 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| ILEUS | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| INGUINAL HERNIA | | | |
| subjects affected / exposed | 56 / 3315 (1.69%) | 57 / 3298 (1.73%) | |
| occurrences causally related to treatment / all | 0 / 58 | 0 / 58 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| INGUINAL HERNIA, OBSTRUCTIVE | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 3 / 3298 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| INTUSSUSCEPTION | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| NECROTISING COLITIS | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 3315 (0.06%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| OESOPHAGEAL MASS | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| RECTAL HAEMORRHAGE | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PANCREATITIS | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| REFLUX OESOPHAGITIS | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| REGURGITATION | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| UMBILICAL HERNIA | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| VOMITING | | | |
| subjects affected / exposed | 5 / 3315 (0.15%) | 3 / 3298 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| CHOLELITHIASIS | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| CHOLESTASIS | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| HEPATIC CYST | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| HYPERBILIRUBINAEMIA | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin and subcutaneous tissue disorders | | | |
| ANGIOEDEMA | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PETECHIAE | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| RASH | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| URTICARIA | | | |
| subjects affected / exposed | 2 / 3315 (0.06%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |

| | | | |
|---|---|---|---|
| URETERIC STENOSIS | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| CRANIOSYNOSTOSIS | | | |
| subjects affected / exposed | 2 / 3315 (0.06%) | 2 / 3298 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| MUSCLE CONTRACTURE | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| OSTEOPENIA | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| ABSCESS NECK | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| ABSCESS LIMB | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| ADENOVIRAL UPPER RESPIRATORY INFECTION | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| BACTERAEMIA | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| BACTERIAL ABSCESS CENTRAL NERVOUS SYSTEM | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| BACTERIAL PYELONEPHRITIS | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| BACTERIAL TRACHEITIS | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| BRONCHITIS | | | |
| subjects affected / exposed | 35 / 3315 (1.06%) | 36 / 3298 (1.09%) | |
| occurrences causally related to treatment / all | 0 / 39 | 0 / 46 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| BRONCHIOLITIS | | | |
| subjects affected / exposed | 71 / 3315 (2.14%) | 78 / 3298 (2.37%) | |
| occurrences causally related to treatment / all | 1 / 87 | 2 / 88 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| BRONCHITIS VIRAL | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 3 / 3298 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| CATHETER SEPSIS | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| BRONCHOPNEUMONIA | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 12 / 3315 (0.36%) | 8 / 3298 (0.24%) | |
| occurrences causally related to treatment / all | 0 / 13 | 0 / 8 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| CENTRAL LINE INFECTION | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| CELLULITIS | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 3 / 3298 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| CLOSTRIDIAL INFECTION | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| CROUP INFECTIOUS | | | |
| subjects affected / exposed | 6 / 3315 (0.18%) | 7 / 3298 (0.21%) | |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 8 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| CYTOMEGALOVIRUS INFECTION | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| DACRYOCYSTITIS | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| DYSENTERY | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| ENTEROBACTER BACTERAEMIA | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| ESCHERICHIA SEPSIS | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| ENTEROCOLITIS VIRAL | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| ESCHERICHIA URINARY TRACT INFECTION | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 2 / 3298 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| EXANTHEMA SUBITUM | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| EXTERNAL EAR CELLULITIS | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| GASTROENTERITIS ADENOVIRUS | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| GASTROENTERITIS | | | |
| subjects affected / exposed | 27 / 3315 (0.81%) | 31 / 3298 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 28 | 1 / 31 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| GASTROENTERITIS ESCHERICHIA COLI | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| GASTROENTERITIS ROTAVIRUS | | | |
| subjects affected / exposed | 13 / 3315 (0.39%) | 21 / 3298 (0.64%) | |
| occurrences causally related to treatment / all | 0 / 15 | 0 / 21 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| GASTROENTERITIS SALMONELLA | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| GASTROENTERITIS VIRAL | | | |
| subjects affected / exposed | 2 / 3315 (0.06%) | 6 / 3298 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| HERPES ZOSTER | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| IMPETIGO | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| INFECTION | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| INFLUENZA | | | |
| subjects affected / exposed | 4 / 3315 (0.12%) | 3 / 3298 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| LOWER RESPIRATORY TRACT INFECTION | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 6 / 3315 (0.18%) | 8 / 3298 (0.24%) | |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 8 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| LARYNGITIS | | | |
| subjects affected / exposed | 5 / 3315 (0.15%) | 5 / 3298 (0.15%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 7 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| LOBAR PNEUMONIA | | | |
| subjects affected / exposed | 2 / 3315 (0.06%) | 3 / 3298 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| LUNG ABSCESS | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| LOWER RESPIRATORY TRACT INFECTION VIRAL | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| MENINGITIS VIRAL | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| LYMPHADENITIS BACTERIAL | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| NASOPHARYNGITIS | | | |
| subjects affected / exposed | 2 / 3315 (0.06%) | 3 / 3298 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| ORAL CANDIDIASIS | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| OSTEOMYELITIS | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| OTITIS MEDIA | | | |
| subjects affected / exposed | 3 / 3315 (0.09%) | 4 / 3298 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| OTITIS MEDIA BACTERIAL | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PARAINFLUENZAE VIRUS INFECTION | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 2 / 3298 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PERTUSSIS | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 2 / 3298 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PHARYNGITIS | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PHARYNGOTONSILLITIS | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PNEUMONIA | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 27 / 3315 (0.81%) | 31 / 3298 (0.94%) | |
| occurrences causally related to treatment / all | 0 / 28 | 0 / 31 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| PNEUMONIA ADENOVIRAL | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PNEUMONIA BACTERIAL | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PNEUMONIA BORDETELLA | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PNEUMONIA INFLUENZAL | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 3 / 3298 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PNEUMONIA RESPIRATORY SYNCYTIAL VIRAL | | | |
| subjects affected / exposed | 2 / 3315 (0.06%) | 10 / 3298 (0.30%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 10 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PNEUMONIA PARAINFLUENZAE VIRAL | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 3 / 3298 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PNEUMONIA VIRAL | | | |
| subjects affected / exposed | 3 / 3315 (0.09%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| POSTOPERATIVE WOUND INFECTION | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PYELONEPHRITIS | | | |
| subjects affected / exposed | 2 / 3315 (0.06%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PYELONEPHRITIS ACUTE | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| RESPIRATORY SYNCYTIAL VIRUS BRONCHIOLITIS | | | |
| subjects affected / exposed | 25 / 3315 (0.75%) | 40 / 3298 (1.21%) | |
| occurrences causally related to treatment / all | 0 / 25 | 0 / 43 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| RESPIRATORY SYNCYTIAL VIRUS INFECTION | | | |
| subjects affected / exposed | 3 / 3315 (0.09%) | 3 / 3298 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| RESPIRATORY TRACT INFECTION | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 2 / 3298 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| RESPIRATORY TRACT INFECTION VIRAL | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| RHINITIS | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 3 / 3298 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| ROTAVIRUS INFECTION | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| SEPSIS | | | |
| subjects affected / exposed | 2 / 3315 (0.06%) | 2 / 3298 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| SINUSITIS | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| STAPHYLOCOCCAL INFECTION | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| TRACHEITIS | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 2 / 3298 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| TRACHEOBRONCHITIS | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 2 / 3298 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| UPPER RESPIRATORY TRACT INFECTION | | | |
| subjects affected / exposed | 14 / 3315 (0.42%) | 22 / 3298 (0.67%) | |
| occurrences causally related to treatment / all | 0 / 14 | 0 / 23 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| URINARY TRACT INFECTION | | | |
| subjects affected / exposed | 10 / 3315 (0.30%) | 7 / 3298 (0.21%) | |
| occurrences causally related to treatment / all | 0 / 10 | 0 / 7 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| URINARY TRACT INFECTION BACTERIAL | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 3315 (0.03%) | 2 / 3298 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| URINARY TRACT INFECTION ENTEROCOCCAL | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| URINARY TRACT INFECTION PSEUDOMONAL | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| UROSEPSIS | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| VARICELLA | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 2 / 3298 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| VIRAL INFECTION | | | |
| subjects affected / exposed | 4 / 3315 (0.12%) | 7 / 3298 (0.21%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 7 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| VIRAL RHINITIS | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| VIRAL UPPER RESPIRATORY TRACT INFECTION | | | |
| subjects affected / exposed | 6 / 3315 (0.18%) | 2 / 3298 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 7 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| WOUND INFECTION | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| ANOREXIA | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| COW'S MILK INTOLERANCE | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 2 / 3298 (0.06%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| DEHYDRATION | | | |
| subjects affected / exposed | 3 / 3315 (0.09%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| FAILURE TO THRIVE | | | |
| subjects affected / exposed | 5 / 3315 (0.15%) | 6 / 3298 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 8 | 0 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| FEEDING DISORDER OF INFANCY OR EARLY CHILDHOOD | | | |
| subjects affected / exposed | 2 / 3315 (0.06%) | 7 / 3298 (0.21%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 7 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| FLUID INTAKE REDUCED | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| FLUID OVERLOAD | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| HYPERCALCAEMIA | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| HYPERNATRAEMIA | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| LACTOSE INTOLERANCE | | | |
| subjects affected / exposed | 0 / 3315 (0.00%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| MALNUTRITION | | | |
| subjects affected / exposed | 2 / 3315 (0.06%) | 1 / 3298 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| WEIGHT GAIN POOR | | | |
| subjects affected / exposed | 2 / 3315 (0.06%) | 3 / 3298 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| ZINC DEFICIENCY | | | |
| subjects affected / exposed | 1 / 3315 (0.03%) | 0 / 3298 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

Frequency threshold for reporting non-serious adverse events: 1 %

| **Non-serious adverse events** | Motavizumab | Palivizumab | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 2784 / 3315 (83.98%) | 2777 / 3298 (84.20%) | |
| Investigations | | | |
| BLOOD UREA INCREASED | | | |
| subjects affected / exposed | 35 / 3315 (1.06%) | 25 / 3298 (0.76%) | |
| occurrences (all) | 35 | 25 | |
| Neoplasms benign, malignant and | | | |

| | | | |
|---|---|---|---|
| unspecified (incl cysts and polyps) | | | |
| HAEMANGIOMA | | | |
| subjects affected / exposed | 29 / 3315 (0.87%) | 38 / 3298 (1.15%) | |
| occurrences (all) | 34 | 41 | |
| Congenital, familial and genetic disorders | | | |
| DACRYOSTENOSIS CONGENITAL | | | |
| subjects affected / exposed | 35 / 3315 (1.06%) | 33 / 3298 (1.00%) | |
| occurrences (all) | 37 | 34 | |
| Blood and lymphatic system disorders | | | |
| ANAEMIA | | | |
| subjects affected / exposed | 66 / 3315 (1.99%) | 73 / 3298 (2.21%) | |
| occurrences (all) | 67 | 75 | |
| General disorders and administration site conditions | | | |
| INJECTION SITE ERYTHEMA | | | |
| subjects affected / exposed | 41 / 3315 (1.24%) | 28 / 3298 (0.85%) | |
| occurrences (all) | 52 | 38 | |
| INJECTION SITE PAIN | | | |
| subjects affected / exposed | 45 / 3315 (1.36%) | 49 / 3298 (1.49%) | |
| occurrences (all) | 81 | 94 | |
| IRRITABILITY | | | |
| subjects affected / exposed | 193 / 3315 (5.82%) | 164 / 3298 (4.97%) | |
| occurrences (all) | 299 | 243 | |
| PYREXIA | | | |
| subjects affected / exposed | 543 / 3315 (16.38%) | 556 / 3298 (16.86%) | |
| occurrences (all) | 718 | 729 | |
| Immune system disorders | | | |
| IMMUNISATION REACTION | | | |
| subjects affected / exposed | 102 / 3315 (3.08%) | 97 / 3298 (2.94%) | |
| occurrences (all) | 138 | 122 | |
| Eye disorders | | | |
| CONJUNCTIVITIS | | | |
| subjects affected / exposed | 246 / 3315 (7.42%) | 251 / 3298 (7.61%) | |
| occurrences (all) | 271 | 285 | |
| Gastrointestinal disorders | | | |
| ABDOMINAL PAIN | | | |
| subjects affected / exposed | 54 / 3315 (1.63%) | 70 / 3298 (2.12%) | |
| occurrences (all) | 55 | 73 | |

| | | | |
|---|---|---|---|
| CONSTIPATION | | | |
| subjects affected / exposed | 234 / 3315 (7.06%) | 227 / 3298 (6.88%) | |
| occurrences (all) | 265 | 262 | |
| DIARRHOEA | | | |
| subjects affected / exposed | 254 / 3315 (7.66%) | 274 / 3298 (8.31%) | |
| occurrences (all) | 295 | 306 | |
| GASTROOESOPHAGEAL REFLUX DISEASE | | | |
| subjects affected / exposed | 190 / 3315 (5.73%) | 190 / 3298 (5.76%) | |
| occurrences (all) | 197 | 198 | |
| FLATULENCE | | | |
| subjects affected / exposed | 126 / 3315 (3.80%) | 119 / 3298 (3.61%) | |
| occurrences (all) | 170 | 135 | |
| UMBILICAL HERNIA | | | |
| subjects affected / exposed | 77 / 3315 (2.32%) | 63 / 3298 (1.91%) | |
| occurrences (all) | 77 | 63 | |
| TEETHING | | | |
| subjects affected / exposed | 299 / 3315 (9.02%) | 282 / 3298 (8.55%) | |
| occurrences (all) | 417 | 408 | |
| VOMITING | | | |
| subjects affected / exposed | 158 / 3315 (4.77%) | 164 / 3298 (4.97%) | |
| occurrences (all) | 174 | 179 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| BRONCHIAL HYPERREACTIVITY | | | |
| subjects affected / exposed | 44 / 3315 (1.33%) | 54 / 3298 (1.64%) | |
| occurrences (all) | 48 | 62 | |
| ASTHMA | | | |
| subjects affected / exposed | 33 / 3315 (1.00%) | 37 / 3298 (1.12%) | |
| occurrences (all) | 37 | 45 | |
| RESPIRATORY DISORDER | | | |
| subjects affected / exposed | 295 / 3315 (8.90%) | 275 / 3298 (8.34%) | |
| occurrences (all) | 380 | 374 | |
| NASAL CONGESTION | | | |
| subjects affected / exposed | 269 / 3315 (8.11%) | 265 / 3298 (8.04%) | |
| occurrences (all) | 318 | 326 | |
| COUGH | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 220 / 3315 (6.64%) | 216 / 3298 (6.55%) | |
| occurrences (all) | 260 | 262 | |
| WHEEZING | | | |
| subjects affected / exposed | 51 / 3315 (1.54%) | 70 / 3298 (2.12%) | |
| occurrences (all) | 61 | 85 | |
| RHINORRHOEA | | | |
| subjects affected / exposed | 99 / 3315 (2.99%) | 92 / 3298 (2.79%) | |
| occurrences (all) | 124 | 112 | |
| Skin and subcutaneous tissue disorders | | | |
| DERMATITIS ATOPIC | | | |
| subjects affected / exposed | 44 / 3315 (1.33%) | 53 / 3298 (1.61%) | |
| occurrences (all) | 48 | 55 | |
| DERMATITIS DIAPER | | | |
| subjects affected / exposed | 177 / 3315 (5.34%) | 192 / 3298 (5.82%) | |
| occurrences (all) | 199 | 233 | |
| DRY SKIN | | | |
| subjects affected / exposed | 35 / 3315 (1.06%) | 25 / 3298 (0.76%) | |
| occurrences (all) | 37 | 26 | |
| ECZEMA | | | |
| subjects affected / exposed | 132 / 3315 (3.98%) | 95 / 3298 (2.88%) | |
| occurrences (all) | 140 | 100 | |
| RASH | | | |
| subjects affected / exposed | 130 / 3315 (3.92%) | 103 / 3298 (3.12%) | |
| occurrences (all) | 147 | 110 | |
| SEBORRHOEIC DERMATITIS | | | |
| subjects affected / exposed | 56 / 3315 (1.69%) | 52 / 3298 (1.58%) | |
| occurrences (all) | 57 | 53 | |
| Psychiatric disorders | | | |
| AGITATION | | | |
| subjects affected / exposed | 35 / 3315 (1.06%) | 47 / 3298 (1.43%) | |
| occurrences (all) | 51 | 61 | |
| Infections and infestations | | | |
| BRONCHIOLITIS | | | |
| subjects affected / exposed | 193 / 3315 (5.82%) | 222 / 3298 (6.73%) | |
| occurrences (all) | 226 | 263 | |
| BRONCHITIS | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 230 / 3315 (6.94%) | 260 / 3298 (7.88%) | |
| occurrences (all) | 328 | 356 | |
| GASTROENTERITIS | | | |
| subjects affected / exposed | 199 / 3315 (6.00%) | 207 / 3298 (6.28%) | |
| occurrences (all) | 212 | 223 | |
| CANDIDIASIS | | | |
| subjects affected / exposed | 58 / 3315 (1.75%) | 79 / 3298 (2.40%) | |
| occurrences (all) | 65 | 93 | |
| LOWER RESPIRATORY TRACT INFECTION | | | |
| subjects affected / exposed | 130 / 3315 (3.92%) | 133 / 3298 (4.03%) | |
| occurrences (all) | 159 | 165 | |
| NASOPHARYNGITIS | | | |
| subjects affected / exposed | 240 / 3315 (7.24%) | 262 / 3298 (7.94%) | |
| occurrences (all) | 325 | 333 | |
| GASTROENTERITIS VIRAL | | | |
| subjects affected / exposed | 40 / 3315 (1.21%) | 32 / 3298 (0.97%) | |
| occurrences (all) | 40 | 36 | |
| PHARYNGITIS | | | |
| subjects affected / exposed | 70 / 3315 (2.11%) | 91 / 3298 (2.76%) | |
| occurrences (all) | 81 | 101 | |
| ORAL CANDIDIASIS | | | |
| subjects affected / exposed | 101 / 3315 (3.05%) | 107 / 3298 (3.24%) | |
| occurrences (all) | 113 | 120 | |
| OTITIS MEDIA | | | |
| subjects affected / exposed | 432 / 3315 (13.03%) | 418 / 3298 (12.67%) | |
| occurrences (all) | 575 | 565 | |
| OTITIS MEDIA ACUTE | | | |
| subjects affected / exposed | 65 / 3315 (1.96%) | 54 / 3298 (1.64%) | |
| occurrences (all) | 83 | 79 | |
| PNEUMONIA | | | |
| subjects affected / exposed | 15 / 3315 (0.45%) | 35 / 3298 (1.06%) | |
| occurrences (all) | 15 | 39 | |
| UPPER RESPIRATORY TRACT INFECTION | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 956 / 3315 (28.84%) | 981 / 3298 (29.75%) | |
| occurrences (all) | 1420 | 1482 | |
| RHINITIS | | | |
| subjects affected / exposed | 440 / 3315 (13.27%) | 444 / 3298 (13.46%) | |
| occurrences (all) | 600 | 593 | |
| VIRAL UPPER RESPIRATORY TRACT INFECTION | | | |
| subjects affected / exposed | 56 / 3315 (1.69%) | 60 / 3298 (1.82%) | |
| occurrences (all) | 64 | 64 | |
| VIRAL INFECTION | | | |
| subjects affected / exposed | 86 / 3315 (2.59%) | 98 / 3298 (2.97%) | |
| occurrences (all) | 103 | 112 | |

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 16 November 2004 | A summary of changes made to create Version 2.0 were as follows. Updated clinical experience with motavizumab. Indicated that liquid palivizumab had now been licensed in the U.S. by FDA. Clarified that blood would be collected to allow for measurement of study drug serum levels and immune reactivity for palivizumab as well as motavizumab. Exclusion criterion was revised as to add varicella zoster immune globulin (VZIG) to the list of polyclonal antibodies whose use within 3 months prior to randomization would result in exclusion. Indicated that receipt of listed concomitant medications had to result in a Medical Monitor review to determine whether or not study drug would be discontinued in the patient in question. The maximum number of days between screening and Study Day 0 was increased from 7 to 30 to allow for more flexibility during screening. Parents/guardians would be provided with study site contact information instead of a telephone calling card. Clarified the evaluation and diagnosis of medically-attended acute respiratory illnesses. Clarified the definition of LRI. Investigational Drug Safety was replaced with other Pharmacovigilance department throughout as the point of contact for serious adverse event (SAE) reporting and day-to-day safety monitoring. |
| 22 June 2005 | The changes were: Updated clinical experience with motavizumab. Revised statistical considerations with the following changes: Updated the non-inferiority margin. Redefining efficacy in terms of relative risk rather than relative efficacy. Clarifying that non-inferiority would be tested prior to superiority. Removing the requirement of a positive point estimate in order to claim non-inferiority. |
| 20 December 2005 | The one change was increasing the target enrollment by approximately 15 percent (%) (from 5750 to 6600). |

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

None reported

## Online references

http://www.ncbi.nlm.nih.gov/pubmed/20008423