



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
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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
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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			
Units: Subjects			

Age Continuous			
Units: months			
arithmetic mean	3.98	3.99	
standard deviation	± 3.78	± 3.75	-
Gender, Male/Female			
Units: participants			
Female	1495	1513	3008
Male	1811	1816	3627
Region of Enrollment			
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]
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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
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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]
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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
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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]
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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
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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]
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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
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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]
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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
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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]
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End point description:

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

End point type	Primary
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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)
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End point description:

LRI was defined as an event of bronchiolitis or pneumonia or the occurrence 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
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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
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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
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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
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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 prescriptions 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
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End point description:

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

End point type	Secondary
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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
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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
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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]
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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
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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 (\pm 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]
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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
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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 (\pm 15.17)			

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 ^[23]
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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
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End point timeframe:

30 days post Dose 2

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	915			
Units: mcg/mL				
arithmetic mean (standard deviation)	64.59 (± 25.6)			

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 ^[24]
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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
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End point timeframe:

30 days post Dose 3

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	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 4

End point title	The Trough Serum Concentrations of Motavizumab at 30 days Post Dose 4 ^[25]
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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
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End point timeframe:

30 days post Dose 4

Notes:

[25] - 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

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

End point title	The Frequency of Medically-Attended Otitis Media (OM) Infections
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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
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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 ^[26]
P-value	= 0.5 ^[27]
Method	Van Elteren test

Notes:

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

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

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 0 - Day 150

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	11.1
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Reporting groups

Reporting group title	Motavizumab
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Reporting group description:

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

Reporting group title	Palivizumab
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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	
VIIIITH 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	
GASTROESOPHAGEAL 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	
BACTERAEemia			

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