Clinical trial results:
A Phase 3 Study of MEDI-524 (Motavizumab), an Enhanced Potency Humanized Respiratory Syncytial Virus (RSV) Monoclonal Antibody, for the Prevention of RSV Disease Among Native American Infants in the Southwestern United States

Summary

EudraCT number	2012-000825-33
Trial protocol	Outside EU/EEA
Global end of trial date	27 December 2010

Results information

Result version number	v2 (current)
This version publication date	24 December 2021
First version publication date	10 February 2016
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	MI-CP117

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00121108
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	MedImmune LLC
Sponsor organisation address	One MedImmune Way, Gaithersburg, United States, MD 20878
Public contact	Global Clinical Lead, MedImmune LLC, 1 877-240-9479, information.center@astrazeneca.com
Scientific contact	Global Clinical Lead, MedImmune LLC, 1 877-240-9479, information.center@astrazeneca.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000352-PIP01-08
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	27 December 2010
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	27 December 2010
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 assess the safety and efficacy of motavizumab compared to placebo when administered monthly by intramuscular (IM) injection for the reduction of the incidence of respiratory syncytial virus (RSV) hospitalization among otherwise healthy Native American infants during their first RSV season.

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	15 November 2004
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy
Long term follow-up duration	3 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 2127
Worldwide total number of subjects	2127
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	841
Infants and toddlers (28 days-23 months)	1286
Children (2-11 years)	0

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: -

Pre-assignment

Screening details:

A total of 2127 participants (710 placebo, 1417 motavizumab) were randomized at 11 sites in the southwestern United States. The number of subjects randomized ranged from 11 to 511 participants per site. Four sites randomized less than 100 participants.

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants received IM dose of placebo matched to motavizumab every 30 days for a maximum of 5 injections (on Days 0, 30, 60, 90, and 120) during the RSV season.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular dose of placebo matched to motavizumab every 30 days for a maximum of 5 injections (on Days 0, 30, 60, 90, and 120) during the RSV season.

Arm title	Motavizumab

Arm description:

Participants received IM dose of motavizumab 15 milligram/Kilogram (mg/kg) every 30 Days for a maximum of 5 injections (on Days 0, 30, 60, 90, and 120) during the RSV season.

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:

Intramuscular dose of motavizumab 15 mg/kg every 30 Days for a maximum of 5 injections (on Days 0, 30, 60, 90, and 120) during the RSV season.

Number of subjects in period 1	Placebo	Motavizumab
Started	710	1417
Completed	589	1192
Not completed	121	225
Adverse event, serious fatal	5	8
Consent withdrawn by subject	106	195
Lost to follow-up	10	22

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received IM dose of placebo matched to motavizumab every 30 days for a maximum of 5 injections (on Days 0, 30, 60, 90, and 120) during the RSV season.	
Reporting group title	Motavizumab
Reporting group description:	
Participants received IM dose of motavizumab 15 milligram/Kilogram (mg/kg) every 30 Days for a maximum of 5 injections (on Days 0, 30, 60, 90, and 120) during the RSV season.	

Reporting group values	Placebo	Motavizumab	Total
Number of subjects	710	1417	2127
Age categorical Units: Subjects			
In Utero	0	0	0
Pre-term newborn - gestational age < 37 wk	0	0	0
Newborns (0-27 days)	271	570	841
Infants and toddlers (28 days-23 months)	439	847	1286
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65 years	0	0	0
Elderly (From 65-84 years)	0	0	0
Elderly 85 years and over	0	0	0
Age Continuous | Units: months			
arithmetic mean	2.13	2.08	
standard deviation	± 1.89	± 1.92	-
Gender, Male/Female Units: Participants			
Male	367	707	1074
Female	343	710	1053
Race/Ethnicity Units: Subjects			
Navajo	576	1149	1725
White Mountain Apache	102	203	305
San Carlos Apache	15	28	43
Zuni	0	1	1
Hopi	8	19	27
Other - Not specified	9	17	26

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants received IM dose of placebo matched to motavizumab every 30 days for a maximum of 5 injections (on Days 0, 30, 60, 90, and 120) during the RSV season.	
Reporting group title	Motavizumab
Reporting group description:	
Participants received IM dose of motavizumab 15 milligram/Kilogram (mg/kg) every 30 Days for a maximum of 5 injections (on Days 0, 30, 60, 90, and 120) during the RSV season.	

Primary: Number of Participants With RSV Hospitalization

End point title	Number of Participants With RSV Hospitalization
End point description:	
An RSV hospitalization is defined as either 1) a respiratory hospitalization with a positive central real-time reverse transcription polymerase chain reaction (RT-PCR) RSV test collected within 3 days of hospitalization or 2) new onset of lower respiratory symptoms in an already hospitalized child, with an objective measure of worsening respiratory status and positive RSV test. The ITT population was analysed which included all participants in the treatment group according to their randomized treatment group.	
End point type	Primary
End point timeframe:	
From study Day 0 through study Day 150	

End point values	Placebo	Motavizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	710	1417		
Units: Participants	80	21		

Statistical analyses

Statistical analysis title	Statistical analysis
Comparison groups	Placebo v Motavizumab
Number of subjects included in analysis	2127
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Fisher exact
Parameter estimate	Relative risk
Point estimate	0.13

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.08
upper limit	0.21

Secondary: Number of Participants With Treatment-emergent Adverse Events (TEAEs) and Treatment-emergent Serious Adverse Events (TESAEs)

End point title	Number of Participants With Treatment-emergent Adverse Events (TEAEs) and Treatment-emergent Serious Adverse Events (TESAEs)

End point description:

An adverse event (AE) is any untoward medical occurrence in a participant who received study drug without
regard to possibility of causal relationship. Serious adverse event is any AE that resulted in death, life threatening, inpatient hospitalization or prolongation of existing hospitalization, persistent or significant disability or incapacity, is a congenital anomaly/birth defect in offspring of a study participant, is an important medical event that may jeopardize the participant or may require medical intervention. The TEAEs are defined as events present at baseline that worsened in intensity after administration of study drug or events absent at baseline that emerged after administration of study drug. Safety population was analysed which included all the participants who received any study drug.

End point type	Secondary

End point timeframe:

From study Day 0 through study Day 150

End point values	Placebo	Motavizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	708	1414		
Units: Participants				
TEAEs	686	1361		
TESAEs	148	212		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With RSV Outpatient Medically Attended Lower Respiratory Illness (MA LRI)

End point title	Number of Participants With RSV Outpatient Medically Attended Lower Respiratory Illness (MA LRI)

End point description:

The RSV outpatient MA LRI was defined as an outpatient medically attended event designated as a lower respiratory illness with a positive RT-PCR RSV test. An LRI event is one that has a medical diagnosis of bronchiolitis or pneumonia. In the absence of such a medical diagnosis, the occurrence of LRI events was determined by the principal investigator after review of the medical record and considering the presence of cough, retractions, rhonchi, wheezing, crackles, or rales, associated with symptoms (by history or clinical findings) of coryza, fever, or apnoea. The ITT population was analysed which included all participants in the treatment group according to their randomized treatment group.

End point type	Secondary

End point timeframe:

From study Day 0 through study Day 150

End point values	Placebo	Motavizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	710	1417		
Units: Participants	71	41		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Medically Attended-Otitis Media (MA-OM) Events

End point title	Number of Participants With Medically Attended-Otitis Media (MA-OM) Events

End point description:

Otitis media (OM) was 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 recorded as a new OM event. The ITT population was analysed which included all participants in the treatment group according to their randomized treatment group.

End point type	Secondary

End point timeframe:

From study Day 0 through study Day 150

End point values	Placebo	Motavizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	710	1417		
Units: Participants	275	532		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Frequency of MA-OM Events

End point title	Number of Participants With Frequency of MA-OM Events

End point description:

Otitis media was recorded as the diagnosis if the following terms were used by the medical care provider: acute OM, acute 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 recorded as a new OM event. Number of participants with frequency of MA-OM events (either 0, 1, 2, 3, or greater than [>] 3) are reported. The ITT population was analysed which included all participants in the treatment group according to their randomized treatment group.

End point type	Secondary

End point timeframe:

From study Day 0 through study Day 150

End point values	Placebo	Motavizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	710	1417		
Units: Participants				
MA-OM: 0	435	885		
MA-OM: 1	190	372		
MA-OM: 2	55	114		
MA-OM: 3	26	32		
MA-OM: >3	4	14		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Medically Attended Wheezing Episodes

End point title	Number of Participants With Medically Attended Wheezing Episodes

End point description:

Wheezing events were included in the analysis of medically-attended wheezing, if the medical care provider documented wheezing in the medical record or records as a discharge diagnosis any of asthma, bronchiolitis, wheezing, or reactive airway disease. A new wheezing episode was recorded as one that occurred >2 weeks after the diagnosis of the previous episode and the medical opinion was that the wheezing does not represent a persistence of the previous episode. Number of participants with greater than or equal to (>=) 1 MA wheezing events and >= 3 MA wheezing events occurring from first through 3 years of age are reported. The ITT population was analysed which included all participants in the treatment group according to their randomized treatment group. Here, "number of subjects analyzed" signified only those participants who were analysed from first year through 3 years.

End point type	Secondary

End point timeframe:

From first year through 3 years

End point values	Placebo	Motavizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	641	1278		
Units: Participants				
>= 1 MA wheezing events	179	342		
>= 3 MA wheezing events	16	35		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Serious Early Childhood Wheezing Episodes

End point title	Number of Participants With Serious Early Childhood Wheezing Episodes

End point description:

Serious early childhood wheezing (SECW) was defined as: three or more medically attended wheezing events over a 12 month period occurring any time from the first through the third birthday, or a need for one or more courses of systemic steroids for a treatment of a medically attended wheezing event from the first through the third birthday, or a need for asthma-controller medication over a 12 month period for at least 3 consecutive months (>= 90 days) or 5 cumulative months (>= 150 days) any time from the first through the third birthday, or at least one inpatient wheezing event from the first through the third birthday. The ITT population included all participants in the treatment group according to their randomized treatment group. Here, "number of subjects analyzed" signified only those participants who were analyzed from first year through 3 years.

End point type	Secondary

End point timeframe:

From first year through 3 years

End point values	Placebo	Motavizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	641	1278		
Units: Participants				
SECW	90	190		
>=3 MA wheezing events over a 12 month period	16	35		
Need of systemic steroids for a MA wheezing event	66	144		
Asthma-controller medication	2	11		
>= 1 hospitalization with MA wheezing	47	91		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Frequency of Medically Attended Wheezing Events

End point title	Number of Participants with Frequency of Medically Attended Wheezing Events

End point description:

Wheezing events were included in the analysis of medically-attended wheezing, if the medical care provider documented wheezing in the medical record or records as a discharge diagnosis any of asthma, bronchiolitis, wheezing, or reactive airway disease. A new wheezing episode was recorded as one that occurred >2 weeks after the diagnosis of the previous episode and the medical opinion is that the wheezing does not represent a persistence of the previous episode. Number of participants with frequency of MA wheezing events (either 0, 1, 2, 3, 4, or greater than or equal to [>=] 5) are reported. The ITT population was analysed which included all participants in the treatment group according to their randomized treatment group.

End point type	Secondary

End point timeframe:

Study Day 0 through 3 years

End point values	Placebo	Motavizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	710	1417		
Units: Participants				
0 events	384	908		
1 event	182	288		
2 event	72	109		
3 events	34	44		
4 events	18	27		
>=5 events	20	41		

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Trough Serum Concentrations of Motavizumab

End point title	Mean Trough Serum Concentrations of Motavizumab[1]

End point description:

The mean trough serum concentrations of motavizumab are reported. Pharmacokinetics (PK) population was analysed which included all participants (in seasons 1 through 3) who received at least 4 doses of motavizumab and had a post-baseline PK measurement available. Here, "n" signified only those participants who had adequate PK samples at the specified time points.

End point type	Secondary

End point timeframe:

Day 0 (pre Dose 1) and Day 120 (Pre Dose 5)

Notes:

[1] - 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: Pharmacokinetic analysis was not planned for Placebo arm but only for Motavizumab arm.

End point values	Motavizumab			
Subject group type	Reporting group			
Number of subjects analysed	629			
Units: µg/mL				
arithmetic mean (standard deviation)				
Day 0 (Pre dose 1) (n=495)	0.003212 (± 0.07147)			
Day 120 (pre dose 5) (n=509)	86.46 (± 31.77)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Positive Anti-Motavizumab Antibodies After Full Dose

End point title	Number of Participants With Positive Anti-Motavizumab Antibodies After Full Dose[2]

End point description:

The number of participants with positive serum antidrug antibodies (ADAs) to motavizumab after full dose are reported. Evaluable population for full dose was analysed which included all participants (in season 1 through 3) who received 4 doses of motavizumab prior to ADA sample collection, and had Day 120 ADA data available. Here, "n" signified only those participants who had adequate ADA samples at the specified time points.

End point type	Secondary

End point timeframe:

Day 0 (Pre Dose 1) and Day 120 (Pre Dose 5)

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Anti-motavizumab antibodies analysis was not planned for Placebo arm but only for Motavizumab arm.

End point values	Motavizumab			
Subject group type	Reporting group			
Number of subjects analysed	670			
Units: Participants				
Day 0 (Pre Dose 1) (n=5)	0			
Day 120 (Pre Dose 5) (n=665)	3			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Positive Anti-Motavizumab Antibodies After Any Dose

End point title	Number of Participants With Positive Anti-Motavizumab Antibodies After Any Dose[3]

End point description:

The number of participants with positive serum ADA to motavizumab after any dose are reported.

Evaluable population for any dose included all participants (in season 1 through 3) who received at least 1 dose of motavizumab prior to ADA sample collection, and had Day 120 ADA data available. Here, "n" signified only those participants who had adequate ADA samples at the specified time points.

End point type	Secondary

End point timeframe:

Day 0 (Pre Dose 1) and Day 120 (Pre Dose 5)

Notes:

[3] - 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: Anti-motavizumab antibodies analysis was not planned for Placebo arm but only for Motavizumab arm.

End point values	Motavizumab			
Subject group type	Reporting group			
Number of subjects analysed	722			
Units: Participants				
Day 0 (Pre Dose 1) (n=5)	0			
Day 120 (Pre Dose 5) (n=717)	3			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From study Day 0 through study Day 150	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	11.1

Reporting groups	
Reporting group title	PLACEBO
Reporting group description:	
Participants received IM dose of placebo matched to motavizumab every 30 days for a maximum of 5 injections (on Days 0, 30, 60, 90, and 120) during the RSV season.	
Reporting group title	MOTAVIZUMAB
Reporting group description:	
Participants received IM dose of motavizumab 15 mg/kg every 30 days for a maximum of 5 injections (on Days 0, 30, 60, 90, and 120) during the RSV season.	

Serious adverse events	PLACEBO	MOTAVIZUMAB	
Total subjects affected by serious adverse events			
subjects affected / exposed	148 / 708 (20.90%)	212 / 1414 (14.99%)	
number of deaths (all causes)	5	8	
number of deaths resulting from adverse events			
Vascular disorders			
VENA CAVA THROMBOSIS			
subjects affected / exposed	0 / 708 (0.00%)	1 / 1414 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
JAUNDICE NEONATAL			
subjects affected / exposed	0 / 708 (0.00%)	1 / 1414 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
FEVER NEONATAL			

subjects affected / exposed	4 / 708 (0.56%)	10 / 1414 (0.71%)	
occurrences causally related to treatment / all	0 / 4	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
PYREXIA			
subjects affected / exposed	3 / 708 (0.42%)	8 / 1414 (0.57%)	
occurrences causally related to treatment / all	0 / 3	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
DRUG HYPERSENSITIVITY			
subjects affected / exposed	0 / 708 (0.00%)	1 / 1414 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPERSENSITIVITY			
subjects affected / exposed	0 / 708 (0.00%)	4 / 1414 (0.28%)	
occurrences causally related to treatment / all	0 / 0	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
MILK ALLERGY			
subjects affected / exposed	0 / 708 (0.00%)	1 / 1414 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Social circumstances			
VICTIM OF CHILD ABUSE			
subjects affected / exposed	0 / 708 (0.00%)	1 / 1414 (0.07%)	
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			
ASPHYXIA			
subjects affected / exposed	1 / 708 (0.14%)	0 / 1414 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
ASTHMA			
subjects affected / exposed	0 / 708 (0.00%)	3 / 1414 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	

BRONCHIAL HYPERREACTIVITY			
subjects affected / exposed	2 / 708 (0.28%)	0 / 1414 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COUGH			
subjects affected / exposed	0 / 708 (0.00%)	1 / 1414 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONITIS			
subjects affected / exposed	3 / 708 (0.42%)	2 / 1414 (0.14%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
BACTERIAL TEST			
subjects affected / exposed	0 / 708 (0.00%)	1 / 1414 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
BLOOD CULTURE POSITIVE			
subjects affected / exposed	1 / 708 (0.14%)	0 / 1414 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
LABORATORY TEST INTERFERENCE			
subjects affected / exposed	1 / 708 (0.14%)	0 / 1414 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
MEDICAL OBSERVATION			
subjects affected / exposed	2 / 708 (0.28%)	0 / 1414 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
HEAD INJURY			
subjects affected / exposed	0 / 708 (0.00%)	3 / 1414 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 2	

POSTOPERATIVE FEVER			
subjects affected / exposed	0 / 708 (0.00%)	1 / 1414 (0.07%)	
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	0 / 708 (0.00%)	1 / 1414 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
THERMAL BURN			
subjects affected / exposed	0 / 708 (0.00%)	2 / 1414 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
BENIGN FAMILIAL NEONATAL CONVULSIONS			
subjects affected / exposed	0 / 708 (0.00%)	1 / 1414 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COMBINED IMMUNODEFICIENCY			
subjects affected / exposed	0 / 708 (0.00%)	1 / 1414 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
FALLOT'S TETRALOGY			
subjects affected / exposed	0 / 708 (0.00%)	1 / 1414 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
MICROVILLOUS INCLUSION DISEASE			
subjects affected / exposed	0 / 708 (0.00%)	1 / 1414 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
CONVULSION			

subjects affected / exposed	2 / 708 (0.28%)	5 / 1414 (0.35%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
DYSKINESIA			
subjects affected / exposed	1 / 708 (0.14%)	0 / 1414 (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 / 708 (0.14%)	1 / 1414 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPOXIC ENCEPHALOPATHY			
subjects affected / exposed	0 / 708 (0.00%)	1 / 1414 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SUBDURAL HYGROMA			
subjects affected / exposed	0 / 708 (0.00%)	1 / 1414 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
CONSTIPATION			
subjects affected / exposed	1 / 708 (0.14%)	0 / 1414 (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	0 / 708 (0.00%)	2 / 1414 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
STOMATITIS			
subjects affected / exposed	0 / 708 (0.00%)	1 / 1414 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			

HYPERBILIRUBINAEMIA			
subjects affected / exposed	6 / 708 (0.85%)	10 / 1414 (0.71%)	
occurrences causally related to treatment / all	0 / 6	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPERBILIRUBINAEMIA NEONATAL			
subjects affected / exposed	1 / 708 (0.14%)	0 / 1414 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
JAUNDICE			
subjects affected / exposed	1 / 708 (0.14%)	1 / 1414 (0.07%)	
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			
DERMATITIS ALLERGIC			
subjects affected / exposed	0 / 708 (0.00%)	1 / 1414 (0.07%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ERYTHEMA			
subjects affected / exposed	0 / 708 (0.00%)	1 / 1414 (0.07%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ERYTHEMA MULTIFORME			
subjects affected / exposed	0 / 708 (0.00%)	1 / 1414 (0.07%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
URTICARIA			
subjects affected / exposed	0 / 708 (0.00%)	1 / 1414 (0.07%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
CRANIOSYNOSTOSIS			
subjects affected / exposed	0 / 708 (0.00%)	1 / 1414 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

MUSCLE TWITCHING			
subjects affected / exposed	0 / 708 (0.00%)	1 / 1414 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SYNOSTOSIS			
subjects affected / exposed	0 / 708 (0.00%)	1 / 1414 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
BACTERIAL PYELONEPHRITIS			
subjects affected / exposed	3 / 708 (0.42%)	3 / 1414 (0.21%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
BRONCHIOLITIS			
subjects affected / exposed	35 / 708 (4.94%)	29 / 1414 (2.05%)	
occurrences causally related to treatment / all	0 / 36	0 / 32	
deaths causally related to treatment / all	0 / 0	0 / 0	
BRONCHITIS			
subjects affected / exposed	1 / 708 (0.14%)	3 / 1414 (0.21%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
BRONCHOPNEUMONIA			
subjects affected / exposed	0 / 708 (0.00%)	1 / 1414 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CELLULITIS			
subjects affected / exposed	0 / 708 (0.00%)	2 / 1414 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
CROUP INFECTIOUS			
subjects affected / exposed	1 / 708 (0.14%)	2 / 1414 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
ESCHERICHIA URINARY TRACT			

INFECTION			
subjects affected / exposed	0 / 708 (0.00%)	2 / 1414 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTROENTERITIS			
subjects affected / exposed	14 / 708 (1.98%)	31 / 1414 (2.19%)	
occurrences causally related to treatment / all	0 / 14	0 / 32	
deaths causally related to treatment / all	0 / 1	0 / 1	
GASTROENTERITIS ROTAVIRUS			
subjects affected / exposed	0 / 708 (0.00%)	3 / 1414 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTROENTERITIS VIRAL			
subjects affected / exposed	0 / 708 (0.00%)	5 / 1414 (0.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
GROIN ABSCESS			
subjects affected / exposed	1 / 708 (0.14%)	0 / 1414 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
INFLUENZA			
subjects affected / exposed	1 / 708 (0.14%)	3 / 1414 (0.21%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
KLEBSIELLA SEPSIS			
subjects affected / exposed	0 / 708 (0.00%)	1 / 1414 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
LOBAR PNEUMONIA			
subjects affected / exposed	3 / 708 (0.42%)	5 / 1414 (0.35%)	
occurrences causally related to treatment / all	0 / 3	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
LOWER RESPIRATORY TRACT INFECTION			

subjects affected / exposed	4 / 708 (0.56%)	8 / 1414 (0.57%)	
occurrences causally related to treatment / all	0 / 4	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
LOWER RESPIRATORY TRACT INFECTION VIRAL			
subjects affected / exposed	1 / 708 (0.14%)	0 / 1414 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
MENINGITIS CANDIDA			
subjects affected / exposed	0 / 708 (0.00%)	1 / 1414 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
MENINGITIS PNEUMOCOCCAL			
subjects affected / exposed	0 / 708 (0.00%)	1 / 1414 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
NASOPHARYNGITIS			
subjects affected / exposed	0 / 708 (0.00%)	1 / 1414 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ORAL HERPES			
subjects affected / exposed	0 / 708 (0.00%)	1 / 1414 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PERINEAL ABSCESS			
subjects affected / exposed	0 / 708 (0.00%)	1 / 1414 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONIA			
subjects affected / exposed	20 / 708 (2.82%)	36 / 1414 (2.55%)	
occurrences causally related to treatment / all	0 / 21	0 / 39	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONIA BACTERIAL			

subjects affected / exposed	1 / 708 (0.14%)	0 / 1414 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONIA HAEMOPHILUS			
subjects affected / exposed	0 / 708 (0.00%)	2 / 1414 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONIA INFLUENZAL			
subjects affected / exposed	1 / 708 (0.14%)	3 / 1414 (0.21%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONIA PNEUMOCOCCAL			
subjects affected / exposed	0 / 708 (0.00%)	1 / 1414 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONIA RESPIRATORY SYNCYTIAL VIRAL			
subjects affected / exposed	6 / 708 (0.85%)	1 / 1414 (0.07%)	
occurrences causally related to treatment / all	0 / 6	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONIA VIRAL			
subjects affected / exposed	0 / 708 (0.00%)	1 / 1414 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PYELONEPHRITIS			
subjects affected / exposed	2 / 708 (0.28%)	4 / 1414 (0.28%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
RESPIRATORY SYNCYTIAL VIRUS BRONCHIOLITIS			
subjects affected / exposed	38 / 708 (5.37%)	16 / 1414 (1.13%)	
occurrences causally related to treatment / all	0 / 39	0 / 17	
deaths causally related to treatment / all	0 / 0	0 / 0	
RESPIRATORY SYNCYTIAL VIRUS INFECTION			

subjects affected / exposed	4 / 708 (0.56%)	3 / 1414 (0.21%)	
occurrences causally related to treatment / all	0 / 5	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 708 (0.00%)	1 / 1414 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	1 / 708 (0.14%)	7 / 1414 (0.50%)	
occurrences causally related to treatment / all	0 / 1	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
URINARY TRACT INFECTION			
subjects affected / exposed	0 / 708 (0.00%)	3 / 1414 (0.21%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
URINARY TRACT INFECTION BACTERIAL			
subjects affected / exposed	0 / 708 (0.00%)	1 / 1414 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
VIRAL INFECTION			
subjects affected / exposed	6 / 708 (0.85%)	5 / 1414 (0.35%)	
occurrences causally related to treatment / all	0 / 6	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
VIRAL PHARYNGITIS			
subjects affected / exposed	0 / 708 (0.00%)	1 / 1414 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
VIRAL UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	1 / 708 (0.14%)	1 / 1414 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			

DEHYDRATION			
subjects affected / exposed	1 / 708 (0.14%)	2 / 1414 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
FAILURE TO THRIVE			
subjects affected / exposed	2 / 708 (0.28%)	1 / 1414 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	PLACEBO	MOTAVIZUMAB	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	682 / 708 (96.33%)	1345 / 1414 (95.12%)	
Investigations			
CARDIAC MURMUR			
subjects affected / exposed	12 / 708 (1.69%)	35 / 1414 (2.48%)	
occurrences (all)	12	35	
Congenital, familial and genetic disorders			
DACRYOSTENOSIS CONGENITAL			
subjects affected / exposed	4 / 708 (0.56%)	23 / 1414 (1.63%)	
occurrences (all)	4	24	
General disorders and administration site conditions			
IRRITABILITY			
subjects affected / exposed	19 / 708 (2.68%)	33 / 1414 (2.33%)	
occurrences (all)	20	33	
PYREXIA			
subjects affected / exposed	160 / 708 (22.60%)	307 / 1414 (21.71%)	
occurrences (all)	193	364	
Ear and labyrinth disorders			
CERUMEN IMPACTION			
subjects affected / exposed	39 / 708 (5.51%)	81 / 1414 (5.73%)	
occurrences (all)	40	94	
EAR PAIN			

subjects affected / exposed	8 / 708 (1.13%)	24 / 1414 (1.70%)	
occurrences (all)	8	24	
Eye disorders			
CONJUNCTIVITIS			
subjects affected / exposed	136 / 708 (19.21%)	271 / 1414 (19.17%)	
occurrences (all)	152	303	
EYE DISCHARGE			
subjects affected / exposed	12 / 708 (1.69%)	21 / 1414 (1.49%)	
occurrences (all)	12	21	
Gastrointestinal disorders			
ABDOMINAL PAIN			
subjects affected / exposed	13 / 708 (1.84%)	26 / 1414 (1.84%)	
occurrences (all)	13	26	
CONSTIPATION			
subjects affected / exposed	57 / 708 (8.05%)	97 / 1414 (6.86%)	
occurrences (all)	61	107	
DIARRHOEA			
subjects affected / exposed	106 / 708 (14.97%)	196 / 1414 (13.86%)	
occurrences (all)	130	230	
ENTERITIS			
subjects affected / exposed	4 / 708 (0.56%)	17 / 1414 (1.20%)	
occurrences (all)	4	17	
FLATULENCE			
subjects affected / exposed	5 / 708 (0.71%)	15 / 1414 (1.06%)	
occurrences (all)	5	16	
GASTROOESOPHAGEAL REFLUX DISEASE			
subjects affected / exposed	10 / 708 (1.41%)	19 / 1414 (1.34%)	
occurrences (all)	10	19	
TEETHING			
subjects affected / exposed	86 / 708 (12.15%)	167 / 1414 (11.81%)	
occurrences (all)	96	178	
VOMITING			
subjects affected / exposed	22 / 708 (3.11%)	49 / 1414 (3.47%)	
occurrences (all)	23	50	
Respiratory, thoracic and mediastinal disorders			

BRONCHIAL HYPERREACTIVITY			
subjects affected / exposed	12 / 708 (1.69%)	18 / 1414 (1.27%)	
occurrences (all)	13	19	
COUGH			
subjects affected / exposed	65 / 708 (9.18%)	149 / 1414 (10.54%)	
occurrences (all)	70	171	
NASAL CONGESTION			
subjects affected / exposed	55 / 708 (7.77%)	128 / 1414 (9.05%)	
occurrences (all)	58	140	
RESPIRATORY DISORDER			
subjects affected / exposed	47 / 708 (6.64%)	93 / 1414 (6.58%)	
occurrences (all)	49	104	
RHINORRHOEA			
subjects affected / exposed	71 / 708 (10.03%)	118 / 1414 (8.35%)	
occurrences (all)	77	123	
Hepatobiliary disorders			
JAUNDICE			
subjects affected / exposed	31 / 708 (4.38%)	45 / 1414 (3.18%)	
occurrences (all)	31	46	
Skin and subcutaneous tissue disorders			
DERMATITIS			
subjects affected / exposed	20 / 708 (2.82%)	39 / 1414 (2.76%)	
occurrences (all)	21	39	
DERMATITIS ATOPIC			
subjects affected / exposed	21 / 708 (2.97%)	24 / 1414 (1.70%)	
occurrences (all)	23	26	
DERMATITIS CONTACT			
subjects affected / exposed	12 / 708 (1.69%)	18 / 1414 (1.27%)	
occurrences (all)	12	18	
DERMATITIS DIAPER			
subjects affected / exposed	149 / 708 (21.05%)	298 / 1414 (21.07%)	
occurrences (all)	183	359	
DRY SKIN			
subjects affected / exposed	21 / 708 (2.97%)	39 / 1414 (2.76%)	
occurrences (all)	22	40	
ECZEMA			

subjects affected / exposed	55 / 708 (7.77%)	80 / 1414 (5.66%)	
occurrences (all)	62	87	
HEAT RASH			
subjects affected / exposed	4 / 708 (0.56%)	15 / 1414 (1.06%)	
occurrences (all)	4	16	
RASH			
subjects affected / exposed	56 / 708 (7.91%)	135 / 1414 (9.55%)	
occurrences (all)	61	146	
RASH GENERALISED			
subjects affected / exposed	3 / 708 (0.42%)	18 / 1414 (1.27%)	
occurrences (all)	3	18	
SEBORRHOEA			
subjects affected / exposed	8 / 708 (1.13%)	11 / 1414 (0.78%)	
occurrences (all)	8	12	
SEBORRHOEIC DERMATITIS			
subjects affected / exposed	18 / 708 (2.54%)	45 / 1414 (3.18%)	
occurrences (all)	18	47	
Infections and infestations			
BRONCHIOLITIS			
subjects affected / exposed	87 / 708 (12.29%)	132 / 1414 (9.34%)	
occurrences (all)	98	146	
BRONCHITIS			
subjects affected / exposed	6 / 708 (0.85%)	19 / 1414 (1.34%)	
occurrences (all)	8	20	
CANDIDA NAPPY RASH			
subjects affected / exposed	30 / 708 (4.24%)	52 / 1414 (3.68%)	
occurrences (all)	30	54	
CROUP INFECTIOUS			
subjects affected / exposed	10 / 708 (1.41%)	27 / 1414 (1.91%)	
occurrences (all)	10	28	
GASTROENTERITIS			
subjects affected / exposed	113 / 708 (15.96%)	196 / 1414 (13.86%)	
occurrences (all)	128	223	
GASTROENTERITIS VIRAL			

subjects affected / exposed	10 / 708 (1.41%)	22 / 1414 (1.56%)	
occurrences (all)	12	24	
IMPETIGO			
subjects affected / exposed	9 / 708 (1.27%)	16 / 1414 (1.13%)	
occurrences (all)	9	17	
LOBAR PNEUMONIA			
subjects affected / exposed	10 / 708 (1.41%)	14 / 1414 (0.99%)	
occurrences (all)	11	14	
LOWER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	53 / 708 (7.49%)	66 / 1414 (4.67%)	
occurrences (all)	58	70	
NASOPHARYNGITIS			
subjects affected / exposed	14 / 708 (1.98%)	38 / 1414 (2.69%)	
occurrences (all)	14	42	
ORAL CANDIDIASIS			
subjects affected / exposed	70 / 708 (9.89%)	118 / 1414 (8.35%)	
occurrences (all)	75	128	
OTITIS EXTERNA			
subjects affected / exposed	3 / 708 (0.42%)	19 / 1414 (1.34%)	
occurrences (all)	3	19	
OTITIS MEDIA			
subjects affected / exposed	268 / 708 (37.85%)	522 / 1414 (36.92%)	
occurrences (all)	381	742	
OTITIS MEDIA ACUTE			
subjects affected / exposed	10 / 708 (1.41%)	17 / 1414 (1.20%)	
occurrences (all)	10	17	
PNEUMONIA			
subjects affected / exposed	45 / 708 (6.36%)	97 / 1414 (6.86%)	
occurrences (all)	50	103	
RESPIRATORY SYNCYTIAL VIRUS BRONCHIOLITIS			
subjects affected / exposed	8 / 708 (1.13%)	8 / 1414 (0.57%)	
occurrences (all)	8	8	
RESPIRATORY SYNCYTIAL VIRUS INFECTION			

subjects affected / exposed	10 / 708 (1.41%)	10 / 1414 (0.71%)	
occurrences (all)	10	10	
RESPIRATORY TRACT INFECTION VIRAL			
subjects affected / exposed	17 / 708 (2.40%)	30 / 1414 (2.12%)	
occurrences (all)	17	32	
RHINITIS			
subjects affected / exposed	8 / 708 (1.13%)	8 / 1414 (0.57%)	
occurrences (all)	8	8	
SKIN CANDIDA			
subjects affected / exposed	11 / 708 (1.55%)	20 / 1414 (1.41%)	
occurrences (all)	11	21	
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	459 / 708 (64.83%)	903 / 1414 (63.86%)	
occurrences (all)	747	1560	
URINARY TRACT INFECTION			
subjects affected / exposed	18 / 708 (2.54%)	22 / 1414 (1.56%)	
occurrences (all)	18	26	
VIRAL INFECTION			
subjects affected / exposed	80 / 708 (11.30%)	175 / 1414 (12.38%)	
occurrences (all)	98	217	
VIRAL SKIN INFECTION			
subjects affected / exposed	15 / 708 (2.12%)	31 / 1414 (2.19%)	
occurrences (all)	15	32	
VIRAL UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	32 / 708 (4.52%)	76 / 1414 (5.37%)	
occurrences (all)	33	78	
Metabolism and nutrition disorders			
DEHYDRATION			
subjects affected / exposed	10 / 708 (1.41%)	18 / 1414 (1.27%)	
occurrences (all)	11	18	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 January 2005	Clinical experience with MEDI-524 Section was updated to reflect the current status of enrollment and results from the Phase 1/2 studies of MEDI-524. Updated study objective and overview to reflect increased monitoring for RSV hospitalizations and medically attended outpatient LRI; the addition of monitoring for non-medically attended wheezing episodes in children who have experienced 3 prior medically attended wheezing episodes while on the study. Timing of the screening visit was changed from "within 7 days before Study Day 0" to "within 60 days before Study Day 0". Follow-up/Evaluations of LRI, Wheezing, OM and Respiratory Hospitalizations Section was updated to include collection of nasopharyngeal samples for RSV for all medically-attended wheezing episode. Safety assessment section was modified to reflect change in the point of contact for serious adverse event reporting and as the party responsible for the day-today safety monitoring of the study.
01 July 2005	The study title was changed to reflect the fact that the study would be conducted in "Native American Indian Infants in the Southwestern United States" rather than being restricted to "Navajo and White Mountain Apache Infants." Dosing with study drug was changed from two RSV seasons for each child to one RSV season for each child. Sample size was changed from approximately 3000 to a minimum of 2100 up to a maximum of 3000. Time period for enrolment was changed from 3-4 RSV seasons to 3 RSV seasons. A futility assessment was added following study completion through Study Day 150 of the second cohort of subjects (Summer 2006), to assess the minimum RSV attack rate in the placebo group and the conditional power calculation of the primary endpoint. An additional analysis was added to determine if RSV immunoprophylaxis during the first RSV season affects subsequent medically-attended LRI or wheezing episodes, after all children in the study have been followed for 3 years. The secondary objective was changed to indicate that wheezing and LRI events would be compared through 3 years of follow-up. Non-medically-attended wheezing episodes would longer be collected. Time period for collection of RSV hospitalization and medically-attended LRI or wheezing episodes were changed.
26 May 2006	Secondary objective was revised to clarify the secondary endpoints and stipulate RSV LRI and wheezing as separate outcomes. Futility assessment to be performed Summer of 2006 would no longer be conducted. Alternatively, an assessment of the blinded events rates was to be conducted after the third season to determine if a fourth season of enrollment was needed to achieve primary and secondary objectives. Respiratory Secretions for RSV detection Section was updated to reflect all future testing of respiratory secretions for RSV be conducted by quantitative polymerase chain reaction.
06 June 2006	Routine Visits and Follow-up through Study Day 150 Section was updated to add that cord blood can only be used to obtain Study Day 0 results if the child was enrolled by 7 days of age. Final Visit for Patients who prematurely discontinue from the Study Section was revised to clarify that the investigator, not the sponsor, was responsible for requesting permission to continue follow-up.

06 June 2007	The study title was changed by replacing Numax™ with Motavizumab and to reflect the fact that the study would be conducted in Native American Infants in the Southwestern United States vs. Native American Indian infants. Clinical Experience with Motavizumab Section was revised with the most current data from recently completed studies (MI-CP118 and MI-CP110) and information from ongoing blinded trials (MI-CP124 and MI-CP127). Rationale for Study Section was updated to detail the conduct and rationale of an interim analysis and possible unbinding of data. Secondary Objectives Section was modified to add seventh objective of "the incidence of asthma in children at 5 years of age who received motavizumab or placebo". Blinding Section was revised by removing all reference to the data monitoring committee, and adding details of the potential unbinding to analyse primary endpoints and secondary endpoints of medically attended LRI and OM, pharmacokinetics, immunogenicity. Routine Visits and Follow-up through Study Day 150 Section was modified to reflect that pre-dose vital sign measurement was extended to within 60 minutes prior to drug dose. Sample Size Section was revised to reflect the updated protocol strategy of conducting an interim analysis. Pulmonary Function Measures Section was revised by specifying that pulmonary function tests would continue unless the analysis of wheezing through 3 years suggests that evaluating the endpoint would be futile. Safety Management During the Study Section was updated to include the content of the DMC reviews for Season 1 and Season 2 (through 15 February 2006) as the concluding paragraph.
18 December 2008	Updated secondary objectives for sample size analysed and for time points. Overview Section was modified. Clarified that the Indian Health Service physician are primary care physicians. Exclusion criteria Section - Exclusion #30 Clarified that for Version 7.0 of the protocol, the follow-up period was being amended to "...through 3 years of age. Blinding Section was updated reflect that interim analysis was performed and data monitoring committee recommended continuation of the study for a fourth season and changed follow-up from "5 years of age" to "3 years of age." In Schedule of Patient Evaluations Section, follow-up was changed from "up to 5 years" to "through 3 years". Routine Laboratory Evaluations Section was updated to clarify that blood samples would only be collected in seasons 1, 2, and 3. Medically Attended Acute Respiratory Illnesses Section clarified that patients in seasons 1 and 2 would be followed for 3 years on study. Definition of wheezing episode Section was changed from 5 years to 3 years. General considerations Section updated number of subjects randomized. Updated the definition of Wheezing Episode, Completion of Primary Study, and Loss to Follow-up visits.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported