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	v1
This version publication date	10 February 2016
First version publication date	10 February 2016

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	Hasan S Jafri, MD, MedImmune LLC, clinicaltrialenquiries@medimmune.com
Scientific contact	Hasan S Jafri, MD, MedImmune LLC, clinicaltrialenquiries@medimmune.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:

Placebo of comparable volume to motavizumab given at 15 milligram per kilogram (mg/kg) administered intramuscularly every 30 days for a maximum of 5 injections during the respiratory syncytial virus (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:

Placebo of comparable volume to motavizumab given at 15 mg/kg administered intramuscularly every 30 days for a maximum of 5 injections during the RSV season.

Arm title	Motavizumab

Arm description:

Motavizumab 15 mg/kg administered intramuscularly every 30 days for a maximum of 5 injections 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:

Motavizumab 15 mg/kg administered intramuscularly every 30 days for a maximum of 5 injections 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:	
Placebo of comparable volume to motavizumab given at 15 milligram per kilogram (mg/kg) administered intramuscularly every 30 days for a maximum of 5 injections during the respiratory syncytial virus (RSV) season.	
Reporting group title	Motavizumab
Reporting group description:	
Motavizumab 15 mg/kg administered intramuscularly every 30 days for a maximum of 5 injections during the RSV season.	

Reporting group values	Placebo	Motavizumab	Total
Number of subjects	710	1417	2127
Age categorical			
Units: Subjects			
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

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Placebo of comparable volume to motavizumab given at 15 milligram per kilogram (mg/kg) administered intramuscularly every 30 days for a maximum of 5 injections during the respiratory syncytial virus (RSV) season.	
Reporting group title	Motavizumab
Reporting group description:	
Motavizumab 15 mg/kg administered intramuscularly every 30 days for a maximum of 5 injections during the RSV season.	
Subject analysis set title	Intent-to-treat (ITT) population analysis: Placebo
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Placebo of comparable volume to motavizumab given at 15 mg/kg administered intramuscularly every 30 days for a maximum of 5 injections during the RSV season. For ITT analyses, the study start (Day 0) was defined as the day of randomization.	
Subject analysis set title	ITT Population Analysis: Motavizumab
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Motavizumab 15 mg/kg administered intramuscularly every 30 days for a maximum of 5 injections during the RSV season. For ITT analyses, the study start (Day 0) was defined as the day of randomization.	
Subject analysis set title	Safety Analysis: Placebo
Subject analysis set type	Safety analysis
Subject analysis set description:	
Placebo of comparable volume to motavizumab given at 15 mg/kg administered intramuscularly every 30 days for a maximum of 5 injections during the RSV season.	
Subject analysis set title	Safety Analysis: Motavizumab
Subject analysis set type	Safety analysis
Subject analysis set description:	
Motavizumab 15 mg/kg administered intramuscularly every 30 days for a maximum of 5 injections during the RSV season.	
Subject analysis set title	Evaluable Population for Any Dose ADA
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Evaluable population for any dose anti-drug antibody (ADA) included participants who received at least 1 dose of motavizumab prior to the collection of ADA sample. Participants who received any motavizumab were counted in the motavizumab group. Only ADA samples collected after the receipt of motavizumab were included in the analysis.	
Subject analysis set title	Evaluable Population for PK: Baseline
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Evaluable population for pharmacokinetic (PK) defined as participants in Seasons 1-3 who were randomized to receive motavizumab, received at least 4 doses. For PK analyses, the study start (Day 0) was defined as the day of the first dose of study product.	
Subject analysis set title	Evaluable Population for PK
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Evaluable population for PK defined as participants (in Seasons 1 through 3) who were randomized to receive motavizumab, received at least 4 doses, and had a post-baseline PK measurement available.	

Primary: Number of Participants Hospitalized With RSV

End point title	Number of Participants Hospitalized With RSV

End point description:

Respiratory hospitalizations with a positive result for real-time reverse transcriptase-polymerase chain reaction (RT-PCR) RSV diagnostic test performed on samples collected within 3 days before or after hospital admission (or date of deterioration, for nosocomial respiratory hospitalizations) were counted in the primary analysis as RSV hospitalizations. Participants were included in the treatment group corresponding to their randomized treatment group. For ITT analyses, the study start (Day 0) was defined as the day of randomization.

End point type	Primary

End point timeframe:

Day 0 through 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 title 1
Comparison groups	Placebo v Motavizumab
Number of subjects included in analysis	2127
Analysis specification	Pre-specified
Analysis type	other
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 an Outpatient Medically Attended Lower Respiratory Illness (MA-LRI) that was Positive for RSV in Seasons 1-4

End point title	Number of Participants With an Outpatient Medically Attended Lower Respiratory Illness (MA-LRI) that was Positive for RSV in Seasons 1-4

End point description:

An RSV outpatient MA-LRI was defined as an outpatient medically attended event designated by the investigator as a lower respiratory illness with a positive RSV RT-PCR performed in the central laboratory. Participants were included in the treatment group corresponding to their randomized treatment group. For ITT analyses, the study start (Day 0) was defined as the day of randomization.

End point type	Secondary

End point timeframe:

Day 0 through 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

Statistical analysis title	Statistical analysis title 1
Comparison groups	Placebo v Motavizumab
Number of subjects included in analysis	2127
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Fisher exact
Parameter estimate	Relative risk
Point estimate	0.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.2
upper limit	0.42

Secondary: Number of Participants with Medically Attended Otitis Media (OM) in Seasons 1-4

End point title	Number of Participants with Medically Attended Otitis Media (OM) in Seasons 1-4

End point description:

Number of participants with any diagnosis of otitis media (OM; including events with only red tympanic membrane and events with perforation or middle ear effusion). Participants were included in the treatment group corresponding to their randomized treatment group. For ITT analyses, the study start (Day 0) was defined as the day of randomization.

End point type	Secondary

End point timeframe:

Day 0 through 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: Frequency of Participants with Events of Medically Attended Otitis Media (MA-OM)

End point title	Frequency of Participants with Events of Medically Attended Otitis Media (MA-OM)

End point description:

A new onset of medically attended OM is defined as a physician-diagnosed OM in either ear after a normal middle ear exam or an episode of acute OM => 21 days after the onset date of the previous episode. Participants were included in the treatment group corresponding to their randomized treatment group. For ITT analyses, the study start (Day 0) was defined as the day of randomization.

End point type	Secondary

End point timeframe:

Seasons 1-4

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

Statistical analysis title	Statistical analysis title 1
Comparison groups	Placebo v Motavizumab
Number of subjects included in analysis	2127
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.521
Method	Cochran-Mantel-Haenszel

Secondary: Frequency of Participants with Medically Attended (MA) Wheezing Events

End point title	Frequency of Participants with Medically Attended (MA) Wheezing Events

End point description:

New wheezing episodes were recorded as those that occurred >2 weeks after the diagnosis of the previous episode and the medical opinion of the investigator was that the wheezing did not represent a persistence of the previous episode. Participants were included in the treatment group corresponding to their randomized treatment group. For ITT analyses, the study start (Day 0) was defined as the day of randomization.

End point type	Secondary

End point timeframe:

Randomization to 3 years old

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

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Anti-Motavizumab Antibodies (Seasons 1-3)

End point title	Number of Participants with Anti-Motavizumab Antibodies (Seasons 1-3)

End point description:

Serum samples with a titer >= 1:30 were considered to be positive for anti-motavizumab antibodies. If the Day 120 sample was positive for anti-motavizumab antibodies, the sample taken prior to Dose 1 was screened for anti-motavizumab antibodies and a confirmatory test was performed on the Day 120 sample. None of the pre-Dose 1 samples were positive for anti-motavizumab antibodies. Results for participants who received any motavizumab were presented.

End point type	Secondary

End point timeframe:

Day 120

End point values	Evaluable Population for Any Dose ADA			
Subject group type	Subject analysis set			
Number of subjects analysed	722			
Units: participants	3			

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline Serum Concentration of Motavizumab Determined in Participants Enrolled in Seasons 1-3

End point title	Baseline Serum Concentration of Motavizumab Determined in Participants Enrolled in Seasons 1-3

End point description:

Participants with a serum concentration < limit of quantitation (LOQ) (LOQ = 1.56 microgram per milliliter [mcg/mL]) at a time point were assigned a value of zero for that time point in the summaries. No imputations were done for missing data. Participants in Seasons 1-3 who were randomized to receive motavizumab, received at least 4 doses, and had a post-baseline pharmacokinetic (PK) measurement available. Results for participants who received any motavizumab were presented.

End point type	Secondary

End point timeframe:

Day 0

End point values	Evaluable Population for PK: Baseline			
Subject group type	Subject analysis set			
Number of subjects analysed	495			
Units: microgram per milliliter				
arithmetic mean (standard deviation)	0.003212 (± 0.07147)			

Statistical analyses

No statistical analyses for this end point

Secondary: Trough Serum Concentration of Motavizumab Determined in Participants Enrolled in Seasons 1-3

End point title	Trough Serum Concentration of Motavizumab Determined in Participants Enrolled in Seasons 1-3

End point description:

Participants with a serum concentration < LOQ (LOQ = 1.56 mcg/mL) at a time point were assigned a value of zero for that time point in the summaries. No imputations were done for missing data. Results for participants who received any motavizumab were presented.

End point type	Secondary

End point timeframe:

30 days post Dose 4

End point values	Evaluable Population for PK			
Subject group type	Subject analysis set			
Number of subjects analysed	509			
Units: mcg/mL				
arithmetic mean (standard deviation)	86.46 (± 31.77)			

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of Participants with Medically Attended (MA) Wheezing Events

End point title	Incidence of Participants with Medically Attended (MA) Wheezing Events

End point description:

New wheezing episodes were recorded as those that occurred >2 weeks after the diagnosis of the previous episode and the medical opinion of the investigator was that the wheezing did not represent a persistence of the previous episode. Participants were included in the treatment group corresponding to their randomized treatment group. Medically attended wheezing events were analyzed using >=1 MA wheezing events and >=3 MA wheezing events over a 12 month period. For ITT analyses, the study start (Day 0) was defined as the day of randomization.

End point type	Secondary

End point timeframe:

Randomization to third birthday

End point values	Placebo	Motavizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	710	1417		
Units: participants				
>=1 MA Wheezing: Randomization - 3 year old	326	509		
>=1 MA Wheezing: >study day 150 - 3 year old	207	383		
>=1 MA Wheezing: 1 - 3 year old	179	342		
>=1 MA Wheezing: 1 - <2 year old	136	278		
>=1 MA Wheezing: 2 - 3 year old	77	143		
>=3 MA Wheezing: Randomization - 3 year old	51	83		
>=3 MA Wheezing: >study day 150 - 3 year old	27	51		
>=3 MA Wheezing: 1 - 3 year old	16	35		
>=3 MA Wheezing: 1 - <2 year old	10	20		

>=3 MA Wheezing: 2 - 3 year old	4	12		

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of Participants with Serious Early Childhood Wheezing (SECW) Events

End point title	Incidence of Participants with Serious Early Childhood Wheezing (SECW) Events

End point description:

Serious early childhood wheezing was defined as: a)Three or more medically attended wheezing events over a 12 month period occurring any time from the first through the third birthday, or b) 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 c) 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 d) At least one inpatient wheezing event from the first through the third birthday. For ITT analyses, the study start (Day 0) was defined as the day of randomization.

End point type	Secondary

End point timeframe:

Randomization to third birthday

End point values	Placebo	Motavizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	710	1417		
Units: participants				
SECW: 1st through 3 year	90	190		
SECW: 1st up to 2 year	69	143		
SECW: 2nd through 3 year	35	79		

Statistical analyses

No statistical analyses for this end point

Adverse events

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

Dictionary used	
Dictionary name	MedDRA
Dictionary version	11.1

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Placebo of comparable volume to motavizumab given at 15 milligram per kilogram (mg/kg) administered intramuscularly every 30 days for a maximum of 5 injections during the respiratory syncytial virus (RSV) season.	
Reporting group title	Motavizumab
Reporting group description:	
Motavizumab 15 mg/kg administered intramuscularly every 30 days for a maximum of 5 injections 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)	2	4	
number of deaths resulting from adverse events	0	0	
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	0 / 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	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	
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	16 / 708 (2.26%)	31 / 1414 (2.19%)	
occurrences causally related to treatment / all	0 / 16	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	2 / 708 (0.28%)	3 / 1414 (0.21%)	
occurrences causally related to treatment / all	0 / 2	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	39 / 708 (5.51%)	16 / 1414 (1.13%)	
occurrences causally related to treatment / all	0 / 40	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	685 / 708 (96.75%)	1354 / 1414 (95.76%)	
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	161 / 708 (22.74%)	307 / 1414 (21.71%)	
occurrences (all)	195	364	
Ear and labyrinth disorders			
Cerumen impaction			
subjects affected / exposed	40 / 708 (5.65%)	81 / 1414 (5.73%)	
occurrences (all)	41	94	
Ear pain			
subjects affected / exposed	8 / 708 (1.13%)	24 / 1414 (1.70%)	
occurrences (all)	8	24	
Eye disorders			
Conjunctivitis			
subjects affected / exposed	137 / 708 (19.35%)	271 / 1414 (19.17%)	
occurrences (all)	153	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	
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	23 / 708 (3.25%)	49 / 1414 (3.47%)	
occurrences (all)	24	50	
Hepatobiliary disorders			
Jaundice			
subjects affected / exposed	31 / 708 (4.38%)	45 / 1414 (3.18%)	
occurrences (all)	31	46	
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	
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	151 / 708 (21.33%)	299 / 1414 (21.15%)	
occurrences (all)	186	360	
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	
Rash			
subjects affected / exposed	57 / 708 (8.05%)	135 / 1414 (9.55%)	
occurrences (all)	62	146	
Rash generalised			
subjects affected / exposed	3 / 708 (0.42%)	18 / 1414 (1.27%)	
occurrences (all)	3	18	
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)	101	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	115 / 708 (16.24%)	196 / 1414 (13.86%)	
occurrences (all)	130	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	
Oral candidiasis			
subjects affected / exposed	70 / 708 (9.89%)	118 / 1414 (8.35%)	
occurrences (all)	75	128	
Nasopharyngitis			

subjects affected / exposed	14 / 708 (1.98%)	38 / 1414 (2.69%)	
occurrences (all)	14	42	
Otitis externa			
subjects affected / exposed	4 / 708 (0.56%)	19 / 1414 (1.34%)	
occurrences (all)	4	19	
Otitis media			
subjects affected / exposed	270 / 708 (38.14%)	522 / 1414 (36.92%)	
occurrences (all)	386	742	
Otitis media acute			
subjects affected / exposed	10 / 708 (1.41%)	17 / 1414 (1.20%)	
occurrences (all)	10	17	
Respiratory tract infection viral			
subjects affected / exposed	17 / 708 (2.40%)	30 / 1414 (2.12%)	
occurrences (all)	17	32	
Pneumonia			
subjects affected / exposed	45 / 708 (6.36%)	97 / 1414 (6.86%)	
occurrences (all)	50	103	
Skin candida			
subjects affected / exposed	11 / 708 (1.55%)	20 / 1414 (1.41%)	
occurrences (all)	11	21	
Upper respiratory tract infection			
subjects affected / exposed	461 / 708 (65.11%)	903 / 1414 (63.86%)	
occurrences (all)	752	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 occurrences (all)	 11 / 708 (1.55%) 12	 18 / 1414 (1.27%) 18	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 January 2005	The major changes were below: Updated for clinical experience with MEDI-524. Updated study objective and overview as - 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. 1) Routine Visits: Timing of the screening visit was changed from Day 0" to "within 60 days before Study Day 0. 2) Follow-up/Evaluations of Lower Respiratory infection (LRI), Wheezing, OM and Respiratory Hospitalizations. 3) Safety Assessment: This was modified as 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 overall reason for the amendment was to include the following changes 1) Study Design Changes: Dosing with study drug was changed; The sample size was changed; The time period for enrolment was changed; A futility assessment was added; An additional analysis was added, to determine if RSV immunoprophylaxis during the first RSV season; comparison of the incidence and frequency of wheezing and LRI were changed; The time period for collection of the following information was changed.
26 May 2006	The overall reason for the amendment was to include the following changes 1) Regarding comparison of the incidence and frequency of medically attended LRIs and wheezing was reworded to only assess LRIs. 2) 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. 3) Respiratory Secretions for RSV Detection: all future testing of respiratory secretions for RSV be conducted by qPCR.
06 June 2006	The overall reason for the amendment was to include the following changes 1) Routine Visits and Follow-up through Study Day 150: This 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. 2) Final Visit for Patients who prematurely discontinue from the Study: This was revised to clarify that the investigator, not the sponsor, is responsible for requesting permission to continue follow-up.
06 June 2007	The overall reason for the amendment was to include the following changes 1) Rationale for Study: To detail the conduct and rationale of an interim analysis and possible unbinding of data. 2) Secondary Objectives: "the incidence of asthma in children at 5 years of age who received motavizumab or placebo," and renumbering the objectives based on collection of the data. 3) Blinding: This was revised by removing all reference to the DMC, and adding details of the potential unbinding to analyse primary endpoints and secondary endpoints of medically attended LRI and OM, pharmacokinetics, immunogenicity. 4) Administration of Study Drug: This was revised by clarifying when it may be appropriate for subsequent injections to be given in the same site. 5) Routine Visits and Follow-up through Study Day 150: Pre-dose vital sign measurement was extended to within 60 minutes prior to drug dose. 6) Pulmonary Function Measures: revised by specifying that pulmonary function tests will continue unless the analysis of wheezing through 3 years suggests that evaluating. 7) Safety Management during the Study was included. 8) Sample Size: revised to reflect the updated protocol strategy of conducting an interim analysis.

18 December 2008	The overall reason for the amendment was to include the following changes 1) Secondary Objectives: changed from "in first Respiratory Syncytia Virus (RSV) season" to "through Day 150"; added "in patients enrolled in seasons 1-3 only"; changed "3 years of follow-up" to "3 years of age". 2) Changes in Study design and eligibility criteria. 3) Follow-up/Evaluation of LRI, Wheezing, OM, and Respiratory Hospitalizations. 4) Final Visit for Patients who Prematurely Discontinue from the Study changed assessment of medically attended acute Lower Respiratory infection (LRI) to occur if discontinuation occurs prior to Study Day 150 but not if discontinuation occurs prior to 3 years of age. 5) Added "central RT-PCR" were added to specify the type of RSV test and changed "within 3 days of hospitalization". 6) Clarified that the IHS physician are primary care physicians. 7) A note was added that Respiratory Secretions for RSV Detection. 8) Routine Laboratory Evaluations: Clarified that blood samples will only be collected in seasons 1, 2, and 3. 9) Medically Attended Acute Respiratory Illnesses: Clarified that patients in seasons 1 and 2 will be followed for 3 years on study. 10) Wheezing Episode Changed from 5 years to 3 years; Changed "research assistant" to "study staff member". 11) Pharmacokinetic and Immunologic Evaluations. 12) Pulmonary Function Test (PFT) measures were deleted. 13) Completion of Primary Study and Loss to Follow-up. 14)Study Reporting Period for Serious Adverse Events. 15) Interruption of Discontinuation of Study Dosing in Individual Patients: Changed from 5 years to 3 years of age. 16) Secondary Endpoints: Clarified that 150 days is from randomization and change 3 years of follow-up to 3 years of age and delete the asthma assessment at age 5.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported