



Clinical trial results:

A Phase 3, Randomized, Double-Blind, Placebo-Controlled Study Evaluating the Efficacy and Safety of a Human Monoclonal Antibody, REGN2222, for the Prevention of Medically Attended RSV Infection in Preterm Infants

Summary

EudraCT number	2015-001714-96
Trial protocol	DK GB HU FI BG ES CZ NL DE
Global end of trial date	26 September 2017

Results information

Result version number	v1 (current)
This version publication date	11 April 2018
First version publication date	11 April 2018

Trial information

Trial identification

Sponsor protocol code	R2222-RSV-1332
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02325791
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Regeneron Pharmaceuticals, Inc.
Sponsor organisation address	777 Old Saw Mill River Rd., Tarrytown, United States, 10591
Public contact	Clinical Trial Management, Regeneron Pharmaceuticals, Inc., clinicaltrials@regeneron.com
Scientific contact	Clinical Trial Management, Regeneron Pharmaceuticals, Inc., clinicaltrials@regeneron.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMA-001747-PIP01-15
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	01 November 2017
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	26 September 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The study consisted of 2 parts: Part A and Part B. The objective of Part A is to determine the Pharmacokinetics (PK) of intramuscular (IM) administration of Suptavumab and Part B is to demonstrate the efficacy of Suptavumab in preventing medically attended respiratory syncytial virus (RSV) infections.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Council for Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 June 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 1
Country: Number of subjects enrolled	Spain: 27
Country: Number of subjects enrolled	Sweden: 3
Country: Number of subjects enrolled	United Kingdom: 14
Country: Number of subjects enrolled	Bulgaria: 173
Country: Number of subjects enrolled	Denmark: 13
Country: Number of subjects enrolled	Finland: 20
Country: Number of subjects enrolled	Germany: 23
Country: Number of subjects enrolled	Hungary: 82
Country: Number of subjects enrolled	United States: 432
Country: Number of subjects enrolled	Australia: 7
Country: Number of subjects enrolled	New Zealand: 25
Country: Number of subjects enrolled	Canada: 15
Country: Number of subjects enrolled	Chile: 127
Country: Number of subjects enrolled	Panama: 5
Country: Number of subjects enrolled	South Africa: 8
Country: Number of subjects enrolled	Turkey: 107
Country: Number of subjects enrolled	Ukraine: 95

Worldwide total number of subjects	1177
EEA total number of subjects	356

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	1177
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
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:

The study was conducted in 2 parts between 22-Jun-2015 and 26-Sep-2017. Part-A of study was conducted at 6 sites in 3 countries and part-B was conducted at 175 sites in 18 countries. Only Part B of the study was conducted in Europe. A total of 23 subjects were enrolled in part-A and a total of 1154 subjects were randomized in part-B.

Pre-assignment

Screening details:

In Part A: 27 subjects were screened, of which 23 received first dose of study drug. In Part B: out of 1154, 1150 subjects received first dose of study drug, of those 1052 continued & received second dose 8 weeks later. Subjects were randomized in 1:1:1 ratio in Part B by gestational age category and region (North America, or rest of the world).

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, Monitor

Blinding implementation details:

Part-A of study was open label where as in Part-B the parent(s) or guardian(s) of study subjects, the principal investigators, and study site personnel were remain blinded to all subject assignments throughout the study. The sponsor's study director, medical monitor, study monitor, and any other sponsor and contract research organization personnel who were in regular contact with the study site were remained blinded to all subject assignments.

Arms

Are arms mutually exclusive?	Yes
Arm title	Part A: Suptavumab 30 mg/kg

Arm description:

Subjects received single dose of suptavumab 30 milligram per kilogram (mg/kg) intramuscularly (IM) on Day 1.

Arm type	Experimental
Investigational medicinal product name	Suptavumab
Investigational medicinal product code	REGN2222
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Single dose of suptavumab 30 mg/kg was administered IM via 1 or 2 simultaneous injections according to the total volume of study drug determined by the subject's body weight. Suptavumab was supplied as a lyophilized powder and was reconstituted with 1.4 milliliter (mL) of sterile water for IM injection, the composition of the drug product was 150 milligram per milliliter (mg/mL) suptavumab.

Arm title	Part B: Placebo matched to Suptavumab
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Arm description:

Subjects received 2 IM doses of placebo matched to Suptavumab. Suptavumab; the first dose on Day 1 and the second dose on Day 57.

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

Dosage and administration details:

Subjects were administered two doses of placebo (matched to suptavumab) 8 weeks apart (q8w).

Arm title	Part B: Suptavumab 30 mg/kg - 1 Dose
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Arm description:

Subjects received single dose of suptavumab 30 mg/kg IM on Day 1 and single dose of placebo matched to suptavumab on Day 57.

Arm type	Experimental
Investigational medicinal product name	Suptavumab
Investigational medicinal product code	REGN2222
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Single dose of suptavumab 30 mg/kg was administered IM via 1 or 2 simultaneous injections according to the total volume of study drug determined by the subject's body weight. Suptavumab was supplied as a lyophilized powder and was reconstituted with 1.4 mL of sterile water for IM injection, the composition of the drug product was 150 mg/mL suptavumab.

Investigational medicinal product name	Placebo (matched to Suptavumab)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects were administered one dose of placebo (matched to suptavumab) on Day 57.

Arm title	Part B: Suptavumab 30 mg/kg - 2 Doses
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Arm description:

Subjects received 2 doses of suptavumab 30 mg/kg IM, the first dose on Day 1 and the second dose on Day 57.

Arm type	Experimental
Investigational medicinal product name	Suptavumab
Investigational medicinal product code	REGN2222
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Suptavumab 30 mg/kg was administered IM via 1 or 2 simultaneous injections according to the total volume of study drug determined by the subject's body weight. Suptavumab was supplied as a lyophilized powder and was reconstituted with 1.4 mL of sterile water for IM injection, the composition of the drug product was 150 mg/mL suptavumab.

Number of subjects in period 1 ^[1]	Part A: Suptavumab 30 mg/kg	Part B: Placebo matched to Suptavumab	Part B: Suptavumab 30 mg/kg - 1 Dose
Started	23	383	385
Completed	23	358	360
Not completed	0	25	25
Physician decision	-	1	1
Consent withdrawn by subject	-	5	8
Death	-	3	-
Adverse event	-	1	1
Lost to follow-up	-	15	14
Protocol deviation	-	-	1

Number of subjects in period 1 ^[1]	Part B: Suptavumab 30 mg/kg - 2 Doses
Started	381
Completed	355
Not completed	26
Physician decision	-
Consent withdrawn by subject	16
Death	1
Adverse event	-
Lost to follow-up	9
Protocol deviation	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: Out of 1177 (Worldwide number enrolled), only 1172 subjects who received the study drug were reported.

Baseline characteristics

Reporting groups

Reporting group title	Part A: Suptavumab 30 mg/kg
Reporting group description: Subjects received single dose of suptavumab 30 milligram per kilogram (mg/kg) intramuscularly (IM) on Day 1.	
Reporting group title	Part B: Placebo matched to Suptavumab
Reporting group description: Subjects received 2 IM doses of placebo matched to Suptavumab. Suptavumab; the first dose on Day 1 and the second dose on Day 57.	
Reporting group title	Part B: Suptavumab 30 mg/kg - 1 Dose
Reporting group description: Subjects received single dose of suptavumab 30 mg/kg IM on Day 1 and single dose of placebo matched to suptavumab on Day 57.	
Reporting group title	Part B: Suptavumab 30 mg/kg - 2 Doses
Reporting group description: Subjects received 2 doses of suptavumab 30 mg/kg IM, the first dose on Day 1 and the second dose on Day 57.	

Reporting group values	Part A: Suptavumab 30 mg/kg	Part B: Placebo matched to Suptavumab	Part B: Suptavumab 30 mg/kg - 1 Dose
Number of subjects	23	383	385
Age categorical Units: Subjects			

Age continuous Units: weeks arithmetic mean standard deviation	6.04 ± 8.284	13.00 ± 6.903	12.59 ± 6.897
Gender categorical Units: Subjects			
Female	9	186	172
Male	14	197	213
Race Units: Subjects			
White	19	338	334
Black or African American	0	32	34
Asian	0	2	3
American Indian or Alaska native	0	0	2
Native hawaiian or other pacific	2	0	0
Other	2	7	9
Not reported	0	4	3
Ethnicity Units: Subjects			
Not hispanic or latino	20	297	300
Hispanic or latino	3	80	81
Not reported	0	6	4

Reporting group values	Part B: Suptavumab	Total	
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Number of subjects	381	1172	
Age categorical			
Units: Subjects			
Age continuous			
Units: weeks			
arithmetic mean	12.75		
standard deviation	± 6.900	-	
Gender categorical			
Units: Subjects			
Female	179	546	
Male	202	626	
Race			
Units: Subjects			
White	326	1017	
Black or African American	35	101	
Asian	3	8	
American Indian or Alaska native	0	2	
Native hawaiian or other pacific	2	4	
Other	11	29	
Not reported	4	11	
Ethnicity			
Units: Subjects			
Not hispanic or latino	302	919	
Hispanic or latino	75	239	
Not reported	4	14	

End points

End points reporting groups

Reporting group title	Part A: Suptavumab 30 mg/kg
Reporting group description: Subjects received single dose of suptavumab 30 milligram per kilogram (mg/kg) intramuscularly (IM) on Day 1.	
Reporting group title	Part B: Placebo matched to Suptavumab
Reporting group description: Subjects received 2 IM doses of placebo matched to Suptavumab. Suptavumab; the first dose on Day 1 and the second dose on Day 57.	
Reporting group title	Part B: Suptavumab 30 mg/kg - 1 Dose
Reporting group description: Subjects received single dose of suptavumab 30 mg/kg IM on Day 1 and single dose of placebo matched to suptavumab on Day 57.	
Reporting group title	Part B: Suptavumab 30 mg/kg - 2 Doses
Reporting group description: Subjects received 2 doses of suptavumab 30 mg/kg IM, the first dose on Day 1 and the second dose on Day 57.	

Primary: Part B: Percentage of Subjects With Medically Attended RSV Infection (Hospitalization or Outpatient Visit With Lower Respiratory Tract Infection [LRTI]) Up to Day 150

End point title	Part B: Percentage of Subjects With Medically Attended RSV Infection (Hospitalization or Outpatient Visit With Lower Respiratory Tract Infection [LRTI]) Up to Day 150 ^[1]
End point description: A medically attended RSV infection defined as an infant with positive RSV test by Reverse-transcriptase polymerase chain reaction (RT-PCR) with any of following events: Hospitalized (on basis of assessment of admitting physician) for RSV infection or outpatient visit (emergency room [ER], urgent care [UC], or pediatric clinic visits [for either a sick or well visit]) with RSV LRTI. An RSV LRTI in an infant: RSV-proven respiratory infection (i.e positive RSV RT-PCR test) with parent(s)/guardian(s) report of cough/difficulty breathing, & with 1 of following signs of LRTI, as assessed by healthcare provider: - lower chest wall indrawing -hypoxemia (peripheral capillary oxygen saturation <95% breathing room air) -Wheezing/crackles. The 150-day efficacy assessment period: first study drug intake through the Day 150 visit. Full analysis set (FAS): all randomized subjects who received any study drug, & is analyzed according to treatment allocated by IVRS/IWRS at randomization (as randomized).	
End point type	Primary
End point timeframe: From first study drug administration up to Day 150	

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: Only arms applicable for this end point are reported.

End point values	Part B: Placebo matched to Suptavumab	Part B: Suptavumab 30 mg/kg - 1 Dose	Part B: Suptavumab 30 mg/kg - 2 Doses	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	383	385	381	
Units: percentage of subjects				
number (not applicable)	8.1	7.7	9.3	

Statistical analyses

Statistical analysis title	Placebo vs suptavumab 30 mg/kg-1 Dose
Statistical analysis description:	
A hierarchical inferential approach was used to control Type-1 error at 0.05 for pairwise comparisons of each suptavumab dose regimen to placebo. Missing values were imputed to Kaplan-Meier (KM) estimate from the placebo group. Randomization strata adjusted in Cochran-Mantel-Haenszel (CMH) test include region (North America vs. Rest of World) & gestational age category (≤ 31 weeks 6 days GA vs ≥ 32 weeks 0 days and ≤ 35 weeks 6 days GA). Threshold for significance at 0.05 level.	
Comparison groups	Part B: Placebo matched to Suptavumab v Part B: Suptavumab 30 mg/kg - 1 Dose
Number of subjects included in analysis	768
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8239 ^[2]
Method	Cochran-Mantel-Haenszel
Parameter estimate	percentage treatment difference
Point estimate	-0.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.318
upper limit	3.438

Notes:

[2] - Analysis performed using CMH statistics with randomization stratum adjusted using Mantel-Haenszel (MH) method to assess pairwise treatment difference (i.e. absolute risk reduction of each suptavumab arm compared to placebo).

Statistical analysis title	Placebo vs suptavumab 30 mg/kg-2 Doses
Statistical analysis description:	
A hierarchical inferential approach was used to control Type-1 error at 0.05 for pairwise comparisons of each suptavumab dose regimen to placebo. Missing values were imputed to KM estimate from the placebo group. Randomization strata adjusted in CMH test include region (North America vs. Rest of World) & gestational age category (≤ 31 weeks 6 days GA vs ≥ 32 weeks 0 days and ≤ 35 weeks 6 days GA). Threshold for significance at 0.05 level.	
Comparison groups	Part B: Suptavumab 30 mg/kg - 2 Doses v Part B: Placebo matched to Suptavumab
Number of subjects included in analysis	764
Analysis specification	Pre-specified
Analysis type	superiority ^[3]
P-value	= 0.5773 ^[4]
Method	Cochran-Mantel-Haenszel
Parameter estimate	percentage treatment difference
Point estimate	1.15

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.898
upper limit	5.201

Notes:

[3] - Analysis performed using CMH statistics with randomization stratum adjusted using MH method to assess pairwise treatment difference (i.e. absolute risk reduction of each suptavumab arm compared to placebo.

[4] - Threshold for significance at 0.05 level.

Secondary: Part A: Percentage of Subjects With Treatment-Emergent Adverse Events (TEAEs)

End point title	Part A: Percentage of Subjects With Treatment-Emergent Adverse Events (TEAEs) ^[5]
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End point description:

Any untoward medical occurrence in subject who received investigational medicinal product (IMP) was considered an adverse event (AE) without regard to possibility of causal relationship with this treatment. TEAEs: AEs that developed/worsened/became serious during on-treatment period (defined as time between the date of first study drug administration & date of end of study/last visit). Serious AE: Any untoward medical occurrence that resulted in any of following outcomes: death, life-threatening, required initial or prolonged in-patient hospitalization, persistent/significant disability/incapacity, congenital anomaly/birth defect, or considered as medically important event. Any TEAE included subjects with both serious & non-serious AEs. National Cancer Institute Common Terminology Criteria (NCI-CTCAE) version 4.03 (Grade 3 [severe] & Grade 4 [life-threatening]) was used in this study to grade clinical AEs. Safety analysis set (SAS) included enrolled subjects who received any dose of suptavumab.

End point type	Secondary
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End point timeframe:

From baseline until Day 150

Notes:

[5] - 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: Only arm applicable for this end point is reported.

End point values	Part A: Suptavumab 30 mg/kg			
Subject group type	Reporting group			
Number of subjects analysed	23			
Units: percentage of subjects				
number (not applicable)				
Any TEAE	69.6			
Any Grade 3/Serious TEAE	4.3			

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Percentage of Subjects Hospitalized With Medically Attended RSV Infection or Outpatient Visit Lower Respiratory Tract Infection (LRTI) or Upper Respiratory Tract Infection (URTI) Up to Day 150

End point title	Part B: Percentage of Subjects Hospitalized With Medically Attended RSV Infection or Outpatient Visit Lower Respiratory Tract Infection (LRTI) or Upper Respiratory Tract Infection (URTI) Up to Day 150 ^[6]
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End point description:

A medically attended RSV infection was defined as an infant with a positive RSV test by RT-PCR with any of the following events: -Hospitalized (on the basis of the assessment of the admitting physician) for RSV infection - or Outpatient visit (ER, UC), or pediatric clinic visits [for either a sick or well visit]] with RSV LRTI. An RSV LRTI in an infant: RSV-proven respiratory infection (i.e, positive RSV RT-PCR test) with parent(s)/guardian(s) report of cough or difficulty breathing, and with 1 of the following signs of LRTI, as assessed by a healthcare provider: -Lower chest wall indrawing -Hypoxemia (peripheral capillary oxygen saturation <95% breathing room air) -Wheezing or crackles. The 150-day efficacy assessment period: first study drug intake through the Day 150 visit. Analysis was performed on FAS population.

End point type	Secondary
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End point timeframe:

From the first study drug administration up to Day 150

Notes:

[6] - 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: Only arms applicable for this end point are reported.

End point values	Part B: Placebo matched to Suptavumab	Part B: Suptavumab 30 mg/kg - 1 Dose	Part B: Suptavumab 30 mg/kg - 2 Doses	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	383	385	381	
Units: percentage of subjects				
number (not applicable)	12.5	11.9	14.5	

Statistical analyses

Statistical analysis title	Placebo vs suptavumab 30 mg/kg- 1 Dose
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Statistical analysis description:

A hierarchical inferential approach was used to control Type-1 error at 0.05 for pairwise comparisons of each suptavumab dose regimen to placebo. Missing values were imputed to KM estimate from the placebo group. Randomization strata adjusted in CMH test include region (North America vs. Rest of World) & gestational age category (<= 31 weeks 6 days GA vs >= 32 weeks 0 days and <= 35 weeks 6 days GA). Threshold for significance at 0.05 level.

Comparison groups	Part B: Placebo matched to Suptavumab v Part B: Suptavumab 30 mg/kg - 1 Dose
Number of subjects included in analysis	768
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7778 ^[7]
Method	Cochran-Mantel-Haenszel
Parameter estimate	percentage treatment difference
Point estimate	-0.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.291
upper limit	3.959

Notes:

[7] - Analysis performed using CMH statistics with randomization stratum adjusted using MH method to assess pairwise treatment difference (i.e. absolute risk reduction of each suptavumab arm compared to placebo.

Statistical analysis title	Placebo vs suptavumab 30 mg/kg- 2 Doses
Statistical analysis description:	
A hierarchical inferential approach was used to control Type-1 error at 0.05 for pairwise comparisons of each suptavumab dose regimen to placebo. Missing values were imputed to KM estimate from the placebo group. Randomization strata adjusted in CMH test include region (North America vs. Rest of World) & gestational age category (≤ 31 weeks 6 days GA vs ≥ 32 weeks 0 days and ≤ 35 weeks 6 days GA). Threshold for significance at 0.05 level.	
Comparison groups	Part B: Placebo matched to Suptavumab v Part B: Suptavumab 30 mg/kg - 2 Doses
Number of subjects included in analysis	764
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4154 ^[8]
Method	Cochran-Mantel-Haenszel
Parameter estimate	percentage treatment difference
Point estimate	2.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.836
upper limit	6.867

Notes:

[8] - Analysis performed using CMH statistics with randomization stratum adjusted using MH method to assess pairwise treatment difference (i.e. absolute risk reduction of each suptavumab arm compared to placebo).

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All Adverse Events (AEs) were collected from signature of the informed consent form up to the final visit (Part A: Day 150 and Part B: Day 237) regardless of seriousness or relationship to investigational product.

Adverse event reporting additional description:

Reported AEs are TEAEs that developed/worsened during the 'on treatment period'. On treatment period for Part A: Day from first dose of drug to the End of study i.e. Day 150 & for Part B: Day from first dose of drug up to the day of last dose of drug plus 180 days. Safety analysis set. Subject data was summarized according to treatment group.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	18.0
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Reporting groups

Reporting group title	Part A: Suptavumab 30 mg/kg
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Reporting group description:

Subjects received single dose of suptavumab 30 milligram per kilogram (mg/kg) intramuscularly (IM) on Day 1.

Reporting group title	Part B: Placebo (matched to suptavumab)
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Reporting group description:

Subjects received 2 doses of placebo matched to suptavumab IM on Day 1 and Day 57.

Reporting group title	Part B: Suptavumab 30 mg/kg- 1 Dose
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Reporting group description:

Subjects received single dose of suptavumab 30 mg/kg IM on Day 1 and single dose of placebo matched to suptavumab on Day 57. Subject data was summarized according to the as treated study treatment group. The impact of this analysis rule was that subjects who were randomized to Suptavumab 2 doses group (Part B: Suptavumab 30 mg/kg) were analyzed for safety in the suptavumab single dose group (Part B: Placebo + Suptavumab 30 mg/kg) if they did not receive the second dose in Part B: Suptavumab 30 mg/kg arm.

Reporting group title	Part B: Suptavumab 30 mg/kg -2 Doses
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Reporting group description:

Subjects received 2 doses of REGN2222 30 mg/kg IM on Day 1 and Day 57. Subject data was summarized according to the as treated study treatment group. The impact of this analysis rule was that subjects who were randomized to REGN2222 2 doses group were analyzed for safety in the suptavumab single dose group (Suptavumab 30 mg/kg + Placebo) if they did not receive the second dose in this arm.

Serious adverse events	Part A: Suptavumab 30 mg/kg	Part B: Placebo (matched to suptavumab)	Part B: Suptavumab 30 mg/kg- 1 Dose
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 23 (0.00%)	44 / 384 (11.46%)	54 / 418 (12.92%)
number of deaths (all causes)	0	2	1
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Eye haemangioma			

subjects affected / exposed	0 / 23 (0.00%)	0 / 384 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemangioma			
subjects affected / exposed	0 / 23 (0.00%)	1 / 384 (0.26%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intra-Abdominal haemangioma			
subjects affected / exposed	0 / 23 (0.00%)	0 / 384 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Crying			
subjects affected / exposed	0 / 23 (0.00%)	1 / 384 (0.26%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Death			
subjects affected / exposed	0 / 23 (0.00%)	0 / 384 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pyrexia			
subjects affected / exposed	0 / 23 (0.00%)	0 / 384 (0.00%)	3 / 418 (0.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Social circumstances			
Child abuse			
subjects affected / exposed	0 / 23 (0.00%)	1 / 384 (0.26%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome			

subjects affected / exposed	0 / 23 (0.00%)	0 / 384 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Apnoea			
subjects affected / exposed	0 / 23 (0.00%)	2 / 384 (0.52%)	2 / 418 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Apnoea neonatal			
subjects affected / exposed	0 / 23 (0.00%)	0 / 384 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory distress			
subjects affected / exposed	0 / 23 (0.00%)	0 / 384 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Respirovirus test positive			
subjects affected / exposed	0 / 23 (0.00%)	1 / 384 (0.26%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Thermal burn			
subjects affected / exposed	0 / 23 (0.00%)	0 / 384 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Amniotic band syndrome			
subjects affected / exposed	0 / 23 (0.00%)	1 / 384 (0.26%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital inguinal hernia			

subjects affected / exposed	0 / 23 (0.00%)	0 / 384 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Macrocephaly			
subjects affected / exposed	0 / 23 (0.00%)	0 / 384 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardio-Respiratory arrest			
subjects affected / exposed	0 / 23 (0.00%)	1 / 384 (0.26%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cyanosis			
subjects affected / exposed	0 / 23 (0.00%)	2 / 384 (0.52%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Brain oedema			
subjects affected / exposed	0 / 23 (0.00%)	1 / 384 (0.26%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Febrile convulsion			
subjects affected / exposed	0 / 23 (0.00%)	1 / 384 (0.26%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotonic-Hyporesponsive episode			
subjects affected / exposed	0 / 23 (0.00%)	0 / 384 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	0 / 23 (0.00%)	1 / 384 (0.26%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	0 / 23 (0.00%)	0 / 384 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukocytosis			
subjects affected / exposed	0 / 23 (0.00%)	0 / 384 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	0 / 23 (0.00%)	0 / 384 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 23 (0.00%)	0 / 384 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 23 (0.00%)	1 / 384 (0.26%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 23 (0.00%)	2 / 384 (0.52%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	0 / 23 (0.00%)	0 / 384 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 23 (0.00%)	0 / 384 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			

subjects affected / exposed	0 / 23 (0.00%)	1 / 384 (0.26%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sandifer's syndrome			
subjects affected / exposed	0 / 23 (0.00%)	1 / 384 (0.26%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Umbilical hernia			
subjects affected / exposed	0 / 23 (0.00%)	0 / 384 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Tubulointerstitial nephritis			
subjects affected / exposed	0 / 23 (0.00%)	1 / 384 (0.26%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Anal abscess			
subjects affected / exposed	0 / 23 (0.00%)	0 / 384 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis bacterial			
subjects affected / exposed	0 / 23 (0.00%)	1 / 384 (0.26%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchiolitis			
subjects affected / exposed	0 / 23 (0.00%)	9 / 384 (2.34%)	10 / 418 (2.39%)
occurrences causally related to treatment / all	0 / 0	0 / 9	0 / 11
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 23 (0.00%)	4 / 384 (1.04%)	2 / 418 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Campylobacter gastroenteritis			

subjects affected / exposed	0 / 23 (0.00%)	0 / 384 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 23 (0.00%)	1 / 384 (0.26%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Corona virus infection			
subjects affected / exposed	0 / 23 (0.00%)	0 / 384 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterovirus infection			
subjects affected / exposed	0 / 23 (0.00%)	0 / 384 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal viral infection			
subjects affected / exposed	0 / 23 (0.00%)	1 / 384 (0.26%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	0 / 23 (0.00%)	0 / 384 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngitis			
subjects affected / exposed	0 / 23 (0.00%)	1 / 384 (0.26%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lobar pneumonia			
subjects affected / exposed	0 / 23 (0.00%)	1 / 384 (0.26%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metapneumovirus infection			

subjects affected / exposed	0 / 23 (0.00%)	0 / 384 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteomyelitis			
subjects affected / exposed	0 / 23 (0.00%)	1 / 384 (0.26%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 23 (0.00%)	1 / 384 (0.26%)	2 / 418 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia respiratory syncytial viral			
subjects affected / exposed	0 / 23 (0.00%)	2 / 384 (0.52%)	2 / 418 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia viral			
subjects affected / exposed	0 / 23 (0.00%)	1 / 384 (0.26%)	2 / 418 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pseudocroup			
subjects affected / exposed	0 / 23 (0.00%)	0 / 384 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	0 / 23 (0.00%)	0 / 384 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus bronchiolitis			
subjects affected / exposed	0 / 23 (0.00%)	5 / 384 (1.30%)	13 / 418 (3.11%)
occurrences causally related to treatment / all	0 / 0	0 / 6	0 / 13
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus bronchitis			

subjects affected / exposed	0 / 23 (0.00%)	1 / 384 (0.26%)	2 / 418 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus infection			
subjects affected / exposed	0 / 23 (0.00%)	1 / 384 (0.26%)	5 / 418 (1.20%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection viral			
subjects affected / exposed	0 / 23 (0.00%)	0 / 384 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rhinitis			
subjects affected / exposed	0 / 23 (0.00%)	1 / 384 (0.26%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rhinovirus infection			
subjects affected / exposed	0 / 23 (0.00%)	1 / 384 (0.26%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rotavirus infection			
subjects affected / exposed	0 / 23 (0.00%)	0 / 384 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal abscess			
subjects affected / exposed	0 / 23 (0.00%)	0 / 384 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 23 (0.00%)	1 / 384 (0.26%)	2 / 418 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Varicella			

subjects affected / exposed	0 / 23 (0.00%)	0 / 384 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 23 (0.00%)	1 / 384 (0.26%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 23 (0.00%)	0 / 384 (0.00%)	2 / 418 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Failure to thrive			
subjects affected / exposed	0 / 23 (0.00%)	1 / 384 (0.26%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Part B: Suptavumab 30 mg/kg -2 Doses		
Total subjects affected by serious adverse events			
subjects affected / exposed	29 / 348 (8.33%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Eye haemangioma			
subjects affected / exposed	1 / 348 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Haemangioma			
subjects affected / exposed	0 / 348 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intra-Abdominal haemangioma			

subjects affected / exposed	0 / 348 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Crying			
subjects affected / exposed	0 / 348 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Death			
subjects affected / exposed	0 / 348 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
subjects affected / exposed	0 / 348 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Social circumstances			
Child abuse			
subjects affected / exposed	0 / 348 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome			
subjects affected / exposed	1 / 348 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Apnoea			
subjects affected / exposed	1 / 348 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Apnoea neonatal			

subjects affected / exposed	0 / 348 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory distress			
subjects affected / exposed	0 / 348 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Investigations			
Respirovirus test positive			
subjects affected / exposed	0 / 348 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Thermal burn			
subjects affected / exposed	1 / 348 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Congenital, familial and genetic disorders			
Amniotic band syndrome			
subjects affected / exposed	0 / 348 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Congenital inguinal hernia			
subjects affected / exposed	0 / 348 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Macrocephaly			
subjects affected / exposed	0 / 348 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardio-Respiratory arrest			

subjects affected / exposed	0 / 348 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cyanosis			
subjects affected / exposed	0 / 348 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Brain oedema			
subjects affected / exposed	0 / 348 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Febrile convulsion			
subjects affected / exposed	0 / 348 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypotonic-Hyporesponsive episode			
subjects affected / exposed	0 / 348 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Seizure			
subjects affected / exposed	1 / 348 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 348 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Leukocytosis			
subjects affected / exposed	1 / 348 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neutropenia			

subjects affected / exposed	1 / 348 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Thrombocytopenia			
subjects affected / exposed	1 / 348 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 348 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			
subjects affected / exposed	0 / 348 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastritis			
subjects affected / exposed	0 / 348 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastroesophageal reflux disease			
subjects affected / exposed	1 / 348 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Inguinal hernia			
subjects affected / exposed	3 / 348 (0.86%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Sandifer's syndrome			
subjects affected / exposed	0 / 348 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Umbilical hernia			

subjects affected / exposed	0 / 348 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Tubulointerstitial nephritis			
subjects affected / exposed	0 / 348 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Anal abscess			
subjects affected / exposed	1 / 348 (0.29%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Arthritis bacterial			
subjects affected / exposed	0 / 348 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bronchiolitis			
subjects affected / exposed	7 / 348 (2.01%)		
occurrences causally related to treatment / all	0 / 7		
deaths causally related to treatment / all	0 / 0		
Bronchitis			
subjects affected / exposed	0 / 348 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Campylobacter gastroenteritis			
subjects affected / exposed	1 / 348 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cellulitis			
subjects affected / exposed	0 / 348 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Corona virus infection			

subjects affected / exposed	1 / 348 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Enterovirus infection				
subjects affected / exposed	0 / 348 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal viral infection				
subjects affected / exposed	0 / 348 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Influenza				
subjects affected / exposed	1 / 348 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Laryngitis				
subjects affected / exposed	0 / 348 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lobar pneumonia				
subjects affected / exposed	0 / 348 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metapneumovirus infection				
subjects affected / exposed	0 / 348 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Osteomyelitis				
subjects affected / exposed	0 / 348 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia				

subjects affected / exposed	1 / 348 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia respiratory syncytial viral				
subjects affected / exposed	1 / 348 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia viral				
subjects affected / exposed	0 / 348 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pseudocroup				
subjects affected / exposed	0 / 348 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis acute				
subjects affected / exposed	1 / 348 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory syncytial virus bronchiolitis				
subjects affected / exposed	2 / 348 (0.57%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Respiratory syncytial virus bronchitis				
subjects affected / exposed	1 / 348 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory syncytial virus infection				
subjects affected / exposed	1 / 348 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory tract infection viral				

subjects affected / exposed	0 / 348 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Rhinitis			
subjects affected / exposed	0 / 348 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Rhinovirus infection			
subjects affected / exposed	0 / 348 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Rotavirus infection			
subjects affected / exposed	1 / 348 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Staphylococcal abscess			
subjects affected / exposed	0 / 348 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	1 / 348 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Varicella			
subjects affected / exposed	0 / 348 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 348 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			

subjects affected / exposed	0 / 348 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Failure to thrive			
subjects affected / exposed	1 / 348 (0.29%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Part A: Suptavumab 30 mg/kg	Part B: Placebo (matched to suptavumab)	Part B: Suptavumab 30 mg/kg- 1 Dose
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 23 (56.52%)	218 / 384 (56.77%)	219 / 418 (52.39%)
Investigations			
Blood alkaline phosphatase increased			
subjects affected / exposed	2 / 23 (8.70%)	0 / 384 (0.00%)	1 / 418 (0.24%)
occurrences (all)	2	0	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 23 (8.70%)	13 / 384 (3.39%)	16 / 418 (3.83%)
occurrences (all)	2	13	16
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 23 (0.00%)	31 / 384 (8.07%)	32 / 418 (7.66%)
occurrences (all)	0	40	37
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 23 (0.00%)	20 / 384 (5.21%)	11 / 418 (2.63%)
occurrences (all)	0	20	13
Diarrhoea			
subjects affected / exposed	0 / 23 (0.00%)	15 / 384 (3.91%)	24 / 418 (5.74%)
occurrences (all)	0	16	25
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 23 (4.35%)	31 / 384 (8.07%)	25 / 418 (5.98%)
occurrences (all)	1	32	25

Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 23 (4.35%)	14 / 384 (3.65%)	24 / 418 (5.74%)
occurrences (all)	1	20	27
Nasal congestion			
subjects affected / exposed	0 / 23 (0.00%)	25 / 384 (6.51%)	24 / 418 (5.74%)
occurrences (all)	0	35	27
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	2 / 23 (8.70%)	12 / 384 (3.13%)	8 / 418 (1.91%)
occurrences (all)	2	13	8
Infections and infestations			
Bronchiolitis			
subjects affected / exposed	2 / 23 (8.70%)	16 / 384 (4.17%)	19 / 418 (4.55%)
occurrences (all)	2	19	27
Bronchitis			
subjects affected / exposed	0 / 23 (0.00%)	24 / 384 (6.25%)	24 / 418 (5.74%)
occurrences (all)	0	32	30
Conjunctivitis			
subjects affected / exposed	1 / 23 (4.35%)	18 / 384 (4.69%)	25 / 418 (5.98%)
occurrences (all)	1	20	28
Nasopharyngitis			
subjects affected / exposed	0 / 23 (0.00%)	53 / 384 (13.80%)	30 / 418 (7.18%)
occurrences (all)	0	73	35
Otitis media			
subjects affected / exposed	0 / 23 (0.00%)	29 / 384 (7.55%)	49 / 418 (11.72%)
occurrences (all)	0	41	84
Rhinitis			
subjects affected / exposed	1 / 23 (4.35%)	14 / 384 (3.65%)	17 / 418 (4.07%)
occurrences (all)	1	15	18
Upper respiratory tract infection			
subjects affected / exposed	3 / 23 (13.04%)	74 / 384 (19.27%)	92 / 418 (22.01%)
occurrences (all)	3	102	127
Viral upper respiratory tract infection			
subjects affected / exposed	3 / 23 (13.04%)	20 / 384 (5.21%)	19 / 418 (4.55%)
occurrences (all)	3	26	26

Non-serious adverse events	Part B: Suptavumab 30 mg/kg -2 Doses		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	198 / 348 (56.90%)		
Investigations			
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 348 (0.29%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	11 / 348 (3.16%)		
occurrences (all)	11		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	22 / 348 (6.32%)		
occurrences (all)	24		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	14 / 348 (4.02%)		
occurrences (all)	14		
Diarrhoea			
subjects affected / exposed	12 / 348 (3.45%)		
occurrences (all)	13		
Gastrooesophageal reflux disease			
subjects affected / exposed	24 / 348 (6.90%)		
occurrences (all)	26		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	23 / 348 (6.61%)		
occurrences (all)	24		
Nasal congestion			
subjects affected / exposed	27 / 348 (7.76%)		
occurrences (all)	33		
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	8 / 348 (2.30%)		
occurrences (all)	8		

Infections and infestations Bronchiolitis subjects affected / exposed occurrences (all) Bronchitis subjects affected / exposed occurrences (all) Conjunctivitis subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all) Otitis media subjects affected / exposed occurrences (all) Rhinitis subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all) Viral upper respiratory tract infection subjects affected / exposed occurrences (all)	 27 / 348 (7.76%) 33 13 / 348 (3.74%) 20 18 / 348 (5.17%) 20 35 / 348 (10.06%) 45 26 / 348 (7.47%) 37 18 / 348 (5.17%) 19 75 / 348 (21.55%) 119 21 / 348 (6.03%) 24		
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More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 April 2015	Following changes are made: • The status of the FIH study was updated by removing "ongoing" • Clarified the primary objective for Part B • Clarified collection of days on supplemental oxygen • Clarified, in Part B, that the permitted windows for prophylaxis will be based on geographical area • Removed references to the study manual • Clarified, in Part A, the process of dosing for the 24 subjects • Clarified physical examination assessment time points, including the addition, in Part A and Part B, of a physical examination postdose • Clarified, in Part A, whether Visit 4 through Visit 6 will be at the clinic (if a blood draw is required) or will be conducted by telephone (if no blood draw is required) • Clarified IDMC review and recommendation to begin enrollment in Part B • Clarified Regeneron PK data review to confirm Part B dose and the addition of PK dosing adjustment rules • In Part B, stratification from country to region was changed • The gestational age categories as ≤ 31 weeks, 6 days GA or from 32 weeks, 0 days to 35 weeks, 6 days GA was clarified • The Part B treatment arms were clarified • In Part B, monitoring of the subject to 1 hour after dosing was clarified • In Part B, the duration of subject participation was changed • Changed the frequency of site contacts to weekly Clarified information concerning the Medical Information Packet by changing the name, by updating the contents of the Medical Information Packet (including removal of swab samples), and by defining the time to the associated follow-up visit • Added the description of the Safety Monitoring Team • Described the unscheduled visit for potential respiratory illness, including assessments • In Part B, the statement regarding availability of study staff by telephone 7 days a week was removed • study stopping rules were added • The countries and regions where study sites may be located were clarified • the study population age was clarified.
08 July 2015	• Extended the Part B Post-Dose Follow-up Period from 93 days to 180 days • Added a section describing the benefit/risk assessment • Updated assessments to be performed at unscheduled visits • Updated the study stopping rules • Clarified that some standard of care treatments are permitted • Included axillary temperature equivalents to rectal temperature • Added a section describing the sponsor's reporting responsibilities • Made minor clarifications to the text

04 August 2015	The following changes were requested by the Pediatric Committee of the European Medicines Agency (PDC) as part of the Pediatric Investigation Plan (PIP) negotiations: • Added 2 secondary endpoints to Part B – Rationale: The addition of secondary endpoints for PK and Antidrug antibody (ADA) titers were to align with agreed PIP. • Added RSV LRTI Analysis and Alternative LRTI Definition Analysis as sensitivity analyses to the primary endpoint – Rationale: To align with the EU protocol and requested by Pediatric Committee (PDCO), respectively The following changes were requested by the Argentinian regulatory authority (ANMAT): • Clarified language in Exclusion Criteria for the Mother – Rationale: To add that infants of mothers who are either 16 years or younger or of an age where they cannot legally provide informed consent in their state/country are excluded. The following additional changes were made: • updated the scientific/medical monitor • clarified the window in Part B during which assessment of primary and secondary clinical endpoints will occur – Rationale: Although no change of the actual window in which primary and secondary endpoint acquisition was made, the change was to clarify that the windows end at different times during the study period. Clarify that subjects who completed Day 150 may be eligible to enroll in a subsequent extension study • Changed the screening period in Part B from 14 to 28 days – Rationale: Based on feedback from study PIs that a longer period from screening to enrollment is required if infants are enrolled in the hospital or neonatal intensive care unit but were enrolled in the study clinic. Removed throat swab collection – Rationale: Based on feedback that because of high sensitivity of RT-PCR for diagnosis of RSV, a throat swab in addition to nose swab is not necessary and could be challenging to collect in some preterm infants.
11 April 2017	Revised the approach of handling of missing data in the primary efficacy analysis as discussed with the United States Food and Drug Administration (US FDA). Specifically, the new statistical approach was directly imputed missing data at Day 150 visit. For those subjects who died prior to Day 150 and the deaths were adjudicated to be RSV related, their missing primary endpoint was imputed as "event occurred". Remaining early termination subjects (including non-RSV deaths) across all treatment groups, was imputed to the average placebo score (estimated placebo event rate). The approach to estimating the placebo event rate was the Kaplan-Meier estimate at Day 150. • Added power calculation for anticipated smaller sample size - Rationale: To understand the impact of the reduced study enrollment on the primary efficacy analysis. • Revised statistical approach to controlling the overall type I error for the primary efficacy analysis. Rationale: To retain sufficient study power for the primary efficacy endpoint given the reduced sample size. To clarify timing of statistical analyses. Specifically, the efficacy analysis was conducted following completion of the 150-day efficacy assessment period by all subjects. This represented the final analysis of all efficacy endpoints. Rationale: Due to the time sensitivity of future study initiation, this supported timely initiation of such studies and avoid long delays waiting for the start of a RSV season.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported