Clinical trial results:
A Prospective, Multicenter, Open-label, Non-comparative Study of Safety and Efficacy of Synagis® in Children at High Risk of Severe Respiratory Syncytial Virus Infection in the Russian Federation

Summary

EudraCT number	2014-004527-42
Trial protocol	Outside EU/EEA
Global end of trial date	13 July 2010

Results information

Result version number	v1 (current)
This version publication date	20 April 2016
First version publication date	14 June 2015

Trial information

Trial identification

Sponsor protocol code	W10-664

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01006629
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AbbVie
Sponsor organisation address	1 North Waukegan Road, North Chicago, IL, United States, 60064
Public contact	Global Medical Information, AbbVie, 001 800-633-9110,
Scientific contact	Global Medical Information, AbbVie, 001 800-633-9110,

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	13 July 2010
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	13 July 2010
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

100 Russian children of 2 years of age and less in high-risk populations (preterm infants [less than or equal to 35 weeks gestational age], infants with bronchopulmonary dysplasia [BPD], and infants with hemodynamically significant congenital heart disease [HSCHD]) will receive palivizumab (Synagis) 15 mg/kg intramuscularly as prophylaxis to severe respiratory syncytial virus (RSV) infection in order to study the safety and efficacy of the drug in Russian subjects.

Protection of trial subjects:

The investigator or his/her representative explained the nature of the study to the subject's parent(s), and answered all questions regarding this study. Prior to any study-related procedures being performed on the subject, the Informed Consent Form was reviewed, signed and dated by the subject's parent(s), the person who administered the informed consent and an impartial witness (a person not involved in the study team at the site and not an Abbott employee). For subjects with two parents, at least one had to sign the consent, stating that the other parent did not object. Participant cards were provided to the subject's parent(s) after the informed consent process, providing contact information for the investigator as well as additional relevant information regarding their child's participation in the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 November 2009
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Russian Federation: 100
Worldwide total number of subjects	100
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)	1
Infants and toddlers (28 days-23 months)	99
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:

Subjects were enrolled into the study in 3 geographic areas of the Russian Federation. Recruitment began in November 2009 and ended in December 2009. Subjects at high risk of severe RSV infection (including preterm infants, infants with BPD, and infants with HSCHD) were identified as candidates for the study on the basis of routine assessments.

Pre-assignment

Screening details:

Screening assessments were conducted at Visit 1 (Day 0) prior to enrollment and study drug administration.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Palivizumab

Arm description:

Palivizumab 15 mg/kg intramuscularly every 30 days for 3 to 5 injections

Arm type	Experimental
Investigational medicinal product name	Palivizumab
Investigational medicinal product code	
Other name	ABT-315 (MEDI-493), Synagis 15 mg/kg intramuscularly
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

palivizumab 15 mg/kg intramuscularly

Number of subjects in period 1	Palivizumab
Started	100
Completed	94
Not completed	6
Adverse event, non-fatal	1
Parent unable to perform site visit	4
Parent refused to continue participation	1

Baseline characteristics

Reporting groups	
Reporting group title	Palivizumab
Reporting group description:	
Palivizumab 15 mg/kg intramuscularly every 30 days for 3 to 5 injections	

Reporting group values	Palivizumab	Total	
Number of subjects	100	100	
Age, Customized Units: participants			
Between 0 and 3 months	28	28	
Between 4 and 6 months	24	24	
Between 7 and 9 months	14	14	
Between 10 and 12 months	7	7	
Between 13 and 15 months	8	8	
Between 16 and 18 months	10	10	
Between 19 and 21 months	5	5	
Between 22 and 24 months	4	4	
Age Continuous Units: months			
arithmetic mean	8.2		
standard deviation	± 6.3	-	
Gender, Male/Female Units: participants			
Female	52	52	
Male	48	48	
Gestational Age, categorical Units: Subjects			
Less than 29 weeks gestational age	23	23	
Between 29 and 32 weeks gestational age	22	22	
Between 33 and 35 weeks gestational age	22	22	
Greater than 35 weeks gestational age	33	33	
Infants born <= 35 weeks gestational age and <= 6 months of age at enrollment Units: Subjects			
Yes	33	33	
No	67	67	
Infants <= 24 months of age at enrollment and with a diagnosis of BPD Units: Subjects			
Yes	46	46	
No	54	54	
Infants <= 24 months of age at enrollment and with HSCHD Units: Subjects			
Yes	30	30	

No	70	70	

Gestational Age			
Gestational age is defined as the time from mother's last menstrual period until birth.			
Units: weeks			
arithmetic mean	33.4		
standard deviation	± 5.1	-	

End points

End points reporting groups

Reporting group title	Palivizumab

Reporting group description:

Palivizumab 15 mg/kg intramuscularly every 30 days for 3 to 5 injections

Primary: Frequency of adverse events

End point title	Frequency of adverse events[1]

End point description:

Treatment-emergent adverse events were defined as those occurring after study drug initiation and within 30 and 100 days after the last dose of study drug. The number of subjects experiencing a serious or nonserious treatment-emergent adverse event within 30 days after the last dose of study drug is summarized. See the Reported Adverse Events section for details.

End point type	Primary

End point timeframe:

Through 30 days following the last injection of palivizumab

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive data were summarized for this endpoint per protocol.

End point values	Palivizumab			
Subject group type	Reporting group			
Number of subjects analysed	100			
Units: participants				
number (not applicable)	41			

Statistical analyses

No statistical analyses for this end point

Primary: Number of hospitalizations due to respiratory syncytial virus (RSV)

End point title	Number of hospitalizations due to respiratory syncytial virus (RSV)[2]

End point description:

Number of subjects experiencing an RSV hospitalization

End point type	Primary

End point timeframe:

Through 30 days following the last injection of palivizumab

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive data were summarized for this endpoint per protocol.

End point values	Palivizumab			
Subject group type	Reporting group			
Number of subjects analysed	100			
Units: participants				
number (confidence interval 95%)	0 (0 to 3.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Total number of RSV hospitalization days

End point title	Total number of RSV hospitalization days

End point description:

All secondary outcome measures were related to hospitalization due to RSV infection. No RSV hospitalizations occurred during the study; therefore, evaluation of the secondary outcome measures was not possible.

End point type	Secondary

End point timeframe:

Through 30 days following the last injection of palivizumab

End point values	Palivizumab			
Subject group type	Reporting group			
Number of subjects analysed	0[3]			
Units: days				
arithmetic mean (standard deviation)	()			

Notes:

[3] - No RSV hospitalizations occurred; therefore, evaluation of the end point was not possible.

Statistical analyses

No statistical analyses for this end point

Secondary: Total RSV hospitalization days with increased supplemental oxygen requirement

End point title	Total RSV hospitalization days with increased supplemental oxygen requirement

End point description:

All secondary outcome measures were related to hospitalization due to RSV infection. No RSV hospitalizations occurred during the study; therefore, evaluation of the secondary outcome measures was not possible.

End point type	Secondary

End point timeframe:

Through 30 days following the last injection of palivizumab

End point values	Palivizumab			
Subject group type	Reporting group			
Number of subjects analysed	0[4]			
Units: days				
arithmetic mean (standard deviation)	()			

Notes:

[4] - No RSV hospitalizations occurred; therefore, evaluation of the end point was not possible.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of intensive care unit (ICU) admissions during RSV hospitalization

End point title	Number of intensive care unit (ICU) admissions during RSV hospitalization

End point description:

Outcome measure refers to the number of subjects admitted to the ICU during RSV hospitalization. No RSV hospitalizations occurred during the study; therefore, evaluation of the secondary outcome measures was not possible.

End point type	Secondary

End point timeframe:

Through 30 days following the last injection of palivizumab

End point values	Palivizumab			
Subject group type	Reporting group			
Number of subjects analysed	0[5]			
Units: participants				
number (not applicable)				

Notes:

[5] - No RSV hospitalizations occurred; therefore, evaluation of the end point was not possible.

Statistical analyses

No statistical analyses for this end point

Secondary: Total days of RSV ICU stay

End point title	Total days of RSV ICU stay

End point description:

All secondary outcome measures were related to hospitalization due to RSV infection. No RSV hospitalizations occurred during the study; therefore, evaluation of the secondary outcome measures was not possible.

End point type	Secondary

End point timeframe:

Through 30 days following the last injection of palivizumab

End point values	Palivizumab			
Subject group type	Reporting group			
Number of subjects analysed	0[6]			
Units: days				
arithmetic mean (standard deviation)	()			

Notes:

[6] - No RSV hospitalizations occurred; therefore, evaluation of the end point was not possible.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Who Received Mechanical Ventilation During RSV Hospitalization

End point title	Number of Subjects Who Received Mechanical Ventilation During RSV Hospitalization

End point description:

All secondary outcome measures were related to hospitalization due to RSV infection. No RSV hospitalizations occurred during the study; therefore, evaluation of the secondary outcome measures was not possible.

End point type	Secondary

End point timeframe:

Through 30 days following the last injection of palivizumab

End point values	Palivizumab			
Subject group type	Reporting group			
Number of subjects analysed	0[7]			
Units: participants				
number (not applicable)				

Notes:

[7] - No RSV hospitalizations occurred; therefore, evaluation of the end point was not possible.

Statistical analyses

No statistical analyses for this end point

Secondary: Total Days of Mechanical Ventilation During RSV Hospitalization

End point title	Total Days of Mechanical Ventilation During RSV Hospitalization

End point description:

All secondary outcome measures were related to hospitalization due to RSV infection. No RSV hospitalizations occurred during the study; therefore, evaluation of the secondary outcome measures was not possible.

End point type	Secondary

End point timeframe:

Through 30 days following the last injection of palivizumab

End point values	Palivizumab			
Subject group type	Reporting group			
Number of subjects analysed	0[8]			
Units: days				
arithmetic mean (standard deviation)	()			

Notes:

[8] - No RSV hospitalizations occurred; therefore, evaluation of the end point was not possible.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From date of first dose of study drug through 100 days after the last dose of study drug

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	13.0

Reporting groups

Reporting group title	Palivizumab

Reporting group description:

Palivizumab 15 mg/kg intramuscularly every 30 days for 3 to 5 injections

Serious adverse events	Palivizumab		
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 100 (10.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Cardiac disorders			
Supraventricular tachycardia			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Enteritis			
subjects affected / exposed	3 / 100 (3.00%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Bronchitis			
subjects affected / exposed	4 / 100 (4.00%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Pneumonia			

subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tonsillitis			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Upper respiratory tract infection			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Palivizumab		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	34 / 100 (34.00%)		
Investigations			
Blood pressure increased			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Thermal burn			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences (all)	1		
Cardiac disorders			
Arrhythmia			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences (all)	1		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences (all)	1		
Immune system disorders			

Food allergy subjects affected / exposed occurrences (all)	1 / 100 (1.00%) 1		
Eye disorders Glaucoma subjects affected / exposed occurrences (all)	1 / 100 (1.00%) 1		
Gastrointestinal disorders Anal stenosis subjects affected / exposed occurrences (all) Teething subjects affected / exposed occurrences (all)	1 / 100 (1.00%) 1 2 / 100 (2.00%) 2		
Respiratory, thoracic and mediastinal disorders Bronchopulmonary dysplasia subjects affected / exposed occurrences (all) Rhinorrhoea subjects affected / exposed occurrences (all) Tonsillar hypertrophy subjects affected / exposed occurrences (all)	3 / 100 (3.00%) 3 1 / 100 (1.00%) 1 1 / 100 (1.00%) 1		
Skin and subcutaneous tissue disorders Dermatitis allergic subjects affected / exposed occurrences (all) Dermatitis contact subjects affected / exposed occurrences (all) Dermatitis atopic subjects affected / exposed occurrences (all)	1 / 100 (1.00%) 1 1 / 100 (1.00%) 1 2 / 100 (2.00%) 2		
Psychiatric disorders			

Nervousness				
subjects affected / exposed	2 / 100 (2.00%)			
occurrences (all)	2			
Infections and infestations				
Ascariasis				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences (all)	1			
Bronchiolitis				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences (all)	1			
Dacryocystitis				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences (all)	1			
Ear infection				
subjects affected / exposed	2 / 100 (2.00%)			
occurrences (all)	2			
Bronchitis				
subjects affected / exposed	3 / 100 (3.00%)			
occurrences (all)	4			
Pharyngitis				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences (all)	1			
Nasopharyngitis				
subjects affected / exposed	2 / 100 (2.00%)			
occurrences (all)	3			
Gastrointestinal infection				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences (all)	1			
Gastroenteritis				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences (all)	1			
Respiratory tract infection				
subjects affected / exposed	2 / 100 (2.00%)			
occurrences (all)	2			
Rhinitis				

subjects affected / exposed	19 / 100 (19.00%)		
occurrences (all)	21		
Respiratory tract infection viral			
subjects affected / exposed	2 / 100 (2.00%)		
occurrences (all)	3		
Upper respiratory tract infection			
subjects affected / exposed	8 / 100 (8.00%)		
occurrences (all)	10		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 May 2009	The purpose of this amendment is to change the first month of enrollment from October to November as well as to clarify to several Inclusion/Exclusion Criteria, Prior and Concomitant therapies and also correct any typographical errors, and make several administrative changes/additions.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

This study had no control group; relative comparisons are only possible with current product information for palivizumab. No RSV hospitalizations occurred during the study; therefore, secondary outcome measures could not be evaluated.

Notes: