Clinical trial results:
A phase I, single-arm, single-center study to investigate safety and reactogenicity of Vaxem HibTM in healthy children aged 16-20 months and infants aged 2-4 months.

Summary

EudraCT number	2014-005036-33
Trial protocol	Outside EU/EEA
Global end of trial date	20 October 2008

Results information

Result version number	v1 (current)
This version publication date	11 May 2016
First version publication date	14 May 2015

Trial information

Trial identification

Sponsor protocol code	M37P1

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00734565
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Vaccines and Diagnostics
Sponsor organisation address	KG, Postfach 1630, Marburg, Germany, 35006
Public contact	Novartis Vaccines, Posting Director, RegistryContactVaccinesUS@novartis.com
Scientific contact	Novartis Vaccines, Posting Director, RegistryContactVaccinesUS@novartis.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	15 July 2009
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	20 October 2008
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine safety and tolerability of Vaxem Hib (Novartis Vaccines) when given to 20 healthy children aged 16-20 months and subsequently to 20 healthy infants aged 2-4 months.

Protection of trial subjects:

This clinical trial was carried out in accordance with relative requirements of Provisions for Drug Registration and Good Clinical Practice (GCP) and Guidelines on Clinical Evaluation of Vaccines issued by State Food and Drug Administration and under the principle of Helsinki Declaration. The study protocol and relevant documents was reviewed and approved by ethics committees in Heibei Provincial Center for Disease Prevention and Control on 25 Jun 2008.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 July 2008
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	China: 40
Worldwide total number of subjects	40
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)	0
Infants and toddlers (28 days-23 months)	40
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 at 1 study center in China.

Pre-assignment

Screening details:

All enrolled subjects were included in the trial.

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

Are arms mutually exclusive?	Yes
Arm title	Vaxem Hib_16 to 20 months

Arm description:

one single dose of 0.5 mL administered by IM;

Arm type	Experimental
Investigational medicinal product name	Vaxem Hib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

one single dose of 0.5 mL adminstered by IM;

Arm title	Vaxem Hib_2 to 4 months

Arm description:

3 doses of 0.5 mL with a time interval of one month between each dose.

Arm type	Experimental
Investigational medicinal product name	Vaxem Hib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

3 doses of 0.5 mL with a time interval of one month between each dose.

Number of subjects in period 1	Vaxem Hib_16 to 20 months	Vaxem Hib_2 to 4 months
Started	20	20
Completed	20	20

Baseline characteristics

Reporting groups	
Reporting group title	Vaxem Hib_16 to 20 months
Reporting group description:	
one single dose of 0.5 mL administered by IM;	
Reporting group title	Vaxem Hib_2 to 4 months
Reporting group description:	
3 doses of 0.5 mL with a time interval of one month between each dose.	

Reporting group values	Vaxem Hib_16 to 20 months	Vaxem Hib_2 to 4 months	Total
Number of subjects	20	20	40
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	20	20	40
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
In stage 2 (Vaxem HIb 2-4 months), one subject aged 5-months, who did not meet the inclusion criteria was included.			
Units: days			
arithmetic mean	17.2	3.3	
standard deviation	± 1.4	± 1	-
Gender categorical Units: Subjects			
Female	9	10	19
Male	11	10	21

End points

End points reporting groups

Reporting group title	Vaxem Hib_16 to 20 months
Reporting group description: one single dose of 0.5 mL administered by IM;	
Reporting group title	Vaxem Hib_2 to 4 months
Reporting group description: 3 doses of 0.5 mL with a time interval of one month between each dose.	
Subject analysis set title	Enrolled Population
Subject analysis set type	Intention-to-treat
Subject analysis set description: All subjects who have been enrolled.	
Subject analysis set title	Exposed Population
Subject analysis set type	Safety analysis
Subject analysis set description: All enrolled subjects who actually received a study vaccination.	
Subject analysis set title	Safety Population
Subject analysis set type	Safety analysis
Subject analysis set description: All subjects enrolled who have received study vaccination and provided any post-baseline safety data.	

Primary: Number of subjects reporting local and systemic reactions during 0-6 days after each vaccination.

End point title	Number of subjects reporting local and systemic reactions during 0-6 days after each vaccination.[1]
End point description: Safety was evaluated as the number of subjects reporting local and systemic reactions occurring between 0-6 days after each vaccination.	
End point type	Primary
End point timeframe: 0-6 days after each vaccination	

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: no statistical analyses required for this endpoint.

End point values	Vaxem Hib_16 to 20 months	Vaxem Hib_2 to 4 months		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	20		
Units: Subjects				
Tenderness	1	1		
Erythema	1	1		
Induration	1	0		
General Reaction	4	5		
Fever	2	1		
Rash	1	2		
Urticaria	1	1		
Other Erythra	0	1		
Change in Eating Habits	1	2		
Sleepiness	0	2		

Unusual Crying	1	3		
Irritability	1	0		
analgesics/antipyretics used	2	1		

Statistical analyses

No statistical analyses for this end point

Primary: Number of unsolicited adverse events occurring throughout the study period.

End point title	Number of unsolicited adverse events occurring throughout the study period.[2]

End point description:

Safety was evaluated as the number of subjects reported unsolicited adverse events throughout the study.

Category 1* (Title) : Withdrawl of study due to drug related adverse events.

Category 2* (Title) : Reduced dose of vaccine for vaccination or disruption and delay of vaccination time due to adverse events.

Category 3* (Title) : Reduced dose of vaccine for vaccination or disruption and delay of vaccination time due to drug-related adverse events.

End point type	Primary

End point timeframe:

Day 1 to Day 90.

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: no statistical analyses required for this endpoint.

End point values	Vaxem Hib_16 to 20 months	Vaxem Hib_2 to 4 months		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	20		
Units: Subjects				
All Adverse events	6	8		
Study related adverse events	0	1		
Serious adverse events	0	0		
Deaths	0	0		
Withdrawal from study due to adverse events	0	0		
Category 1* (see description for title)	0	0		
Category 2* (see description for title)	0	0		
Category 3* (see description for title)	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited adverse events were collected from Day 0-6 after vaccination; Unsolicited adverse events were collected from day 1 to 90.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	Vaxem Hib_16 to 20 months

Reporting group description:

one single dose of 0.5 mL administered by IM;

Reporting group title	Vaxem Hib_2 to 4 months

Reporting group description:

3 doses of 0.5 mL with a time interval of one month between each dose.

Serious adverse events	Vaxem Hib_16 to 20 months	Vaxem Hib_2 to 4 months	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Vaxem Hib_16 to 20 months	Vaxem Hib_2 to 4 months	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 20 (30.00%)	7 / 20 (35.00%)	
Nervous system disorders			
Somnolence			
subjects affected / exposed	0 / 20 (0.00%)	2 / 20 (10.00%)	
occurrences (all)	0	4	
General disorders and administration site conditions			
Crying			
subjects affected / exposed	1 / 20 (5.00%)	3 / 20 (15.00%)	
occurrences (all)	1	3	
Pyrexia			

subjects affected / exposed occurrences (all)	3 / 20 (15.00%) 3	1 / 20 (5.00%) 2	
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all)	 0 / 20 (0.00%) 0	 3 / 20 (15.00%) 3	
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all)	 1 / 20 (5.00%) 2	 2 / 20 (10.00%) 2	
Psychiatric disorders Eating disorder subjects affected / exposed occurrences (all)	 1 / 20 (5.00%) 1	 2 / 20 (10.00%) 3	
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	 4 / 20 (20.00%) 4	 5 / 20 (25.00%) 5	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 July 2008	Change in route of administration.

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.

N/A

Notes: