Clinical trial results:
A Phase IIIb, Controlled, Open Label, Single-Center, Persistency, Extension study in Chinese children after a 2 + 1 dose series of either CRM197- conjugate Haemophilus influenzae type b vaccine or tetanus toxoid-conjugate Haemophilus influenzae type b vaccine

Summary

EudraCT number	2015-001453-32
Trial protocol	Outside EU/EEA
Global end of trial date	29 January 2015

Results information

Result version number	v1 (current)
This version publication date	12 December 2016
First version publication date	28 June 2015

Trial information

Trial identification

Sponsor protocol code	V37_07E2

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02139228
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Vaccines and Diagnostics Srl
Sponsor organisation address	Via Fiorentina, 1, Siena, Italy, 53100
Public contact	Posting Director, Novartis Vaccines and Diagnostics Srl, RegistryContactVaccinesUS@novartis.com
Scientific contact	Posting Director, Novartis Vaccines and Diagnostics Srl, 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	05 May 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 December 2014
Global end of trial reached?	Yes
Global end of trial date	29 January 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Immunogenicity Objective:
To assess anti- PRP antibodies persistency in children participating in previous V37_07E1 trial (EUDRACT number:2014-005135-13), approximately 4 years after booster vaccination with either Hib-CRM197 or Hib-TT.

Protection of trial subjects:

This study was conducted in accordance with relevant requirements specified in Provisions for Drug Registration (PDR), Good Clinical Practice (GCP), GCP for vaccine trials issued by the CFDA. The Technical Guidelines on Clinical Trial of Vaccine were executed by closely following the principles of the Helsinki Declaration. The trial was performed under the organization of Hebei Center for Disease Control, and its trial protocol, along with relevant documents, was approved by the Ethics Committee of Hebei Center for Disease Control on 21 APR 14 after review. The study was conducted by scientifically and medically qualified persons; and each subject' parents or legal guardian signed the Informed Consent Form before any protocol procedure was performed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	29 November 2014
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: 426
Worldwide total number of subjects	426
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)	0
Children (2-11 years)	426
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:

One centre in China

Pre-assignment

Screening details:

All subjects enrolled into the parent V37_07E1 (EUDRACT number:2014-005135-13) study were invited to participate in the trial

Period 1

Period 1 title	Enrolled (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	Hib CRM197

Arm description:

Subjects treated with 3 doses of CRM 197 –conjugate Haemophilus influenzae type b vaccine (study vaccine): 2 doses given one month apart during study V37_07 (2014-005136-33) and a booster dose of the same vaccine six month after, during study V37_07E1 (2014-005135-13).

No vaccine was administered during this trial

Arm type	no product administered
Investigational medicinal product name	No product was administered in this extension study
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Route of administration not applicable

Arm title	Hib TT

Arm description:

Subjects treated with 3 doses of Tetanus Toxoid-conjugate Haemophilus influenzae type b vaccine (comparator vaccine): 2 doses given one month apart during study V37_07 (2014-005136-33) and a booster dose of the same vaccine six month after, during study V37_07E1 (2014-005135-13).

No vaccine was administered during this trial

Arm type	no product administered

No investigational medicinal product assigned in this arm

Number of subjects in period 1	Hib CRM197	Hib TT
Started	215	211
Completed	215	211

Baseline characteristics

Reporting groups	
Reporting group title	Hib CRM197

Reporting group description:

Subjects treated with 3 doses of CRM 197 –conjugate Haemophilus influenzae type b vaccine (study vaccine): 2 doses given one month apart during study V37_07 (2014-005136-33) and a booster dose of the same vaccine six month after, during study V37_07E1 (2014-005135-13).

No vaccine was administered during this trial

Reporting group title	Hib TT

Reporting group description:

Subjects treated with 3 doses of Tetanus Toxoid-conjugate Haemophilus influenzae type b vaccine (comparator vaccine): 2 doses given one month apart during study V37_07 (2014-005136-33) and a booster dose of the same vaccine six month after, during study V37_07E1 (2014-005135-13).

No vaccine was administered during this trial

Reporting group values	Hib CRM197	Hib TT	Total
Number of subjects	215	211	426
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	5	5	
standard deviation	± 0	± 0	-
Gender categorical Units: Subjects			
Female	99	106	205
Male	116	105	221

End points

End points reporting groups

Reporting group title	Hib CRM197

Reporting group description:

Subjects treated with 3 doses of CRM 197 –conjugate Haemophilus influenzae type b vaccine (study vaccine): 2 doses given one month apart during study V37_07 (2014-005136-33) and a booster dose of the same vaccine six month after, during study V37_07E1 (2014-005135-13).

No vaccine was administered during this trial

Reporting group title	Hib TT

Reporting group description:

Subjects treated with 3 doses of Tetanus Toxoid-conjugate Haemophilus influenzae type b vaccine (comparator vaccine): 2 doses given one month apart during study V37_07 (2014-005136-33) and a booster dose of the same vaccine six month after, during study V37_07E1 (2014-005135-13).

No vaccine was administered during this trial

Subject analysis set title	Enrolled Set
Subject analysis set type	Per protocol

Subject analysis set description:

All screened subjects for which the parent or legal guardian provided the informed consent and provided demographic and/or other baseline screening assessments assigned a study subject ID.

Subject analysis set title	Per Protocol (PP) Set Immunogenicity
Subject analysis set type	Per protocol

Subject analysis set description:

All subjects in the All Enrolled Set with no reportable protocol deviations

Primary: Geometric Mean Anti-PRP Concentrations at Day 1(approximately 4 years post booster dose administered in study V37_07E1)

End point title	Geometric Mean Anti-PRP Concentrations at Day 1(approximately 4 years post booster dose administered in study V37_07E1)

End point description:

Immunogenicity was measured as geometric mean of Anti- Polyribosyl Ribitol Phosphate (PRP) concentrations, approximately 4 years after booster vaccination with either Hib-CRM197 or Hib-TT in children participating in previous V37_07E1 trial (2014-005135-13).
Analysis was evaluated on the PPS (i.e. All subjects in the All Enrolled Set with no reportable protocol deviations).

End point type	Primary

End point timeframe:

At Day 1 (approximately 4 years post booster dose administered in study V37_07E1).

End point values	Hib CRM197	Hib TT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	215	211		
Units: Concentration in µg/mL				
geometric mean (confidence interval 95%)				
Day 1	2.66 (2 to 3.54)	5.05 (3.97 to 6.42)		

Statistical analyses

Statistical analysis title	Ratios of Geometric Mean Anti-PRP Concentrations
Comparison groups	Hib CRM197 v Hib TT
Number of subjects included in analysis	426
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	Vaccine Group Ratios
Point estimate	0.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.36
upper limit	0.76

Secondary: Percentages of Subjects with Anti-PRP Concentrations ≥1.0 µg/mL and ≥0.15 µg/mL at Day 1 (approximately 4 years post booster dose administered in study V37_07E1)

End point title	Percentages of Subjects with Anti-PRP Concentrations ≥1.0 µg/mL and ≥0.15 µg/mL at Day 1 (approximately 4 years post booster dose administered in study V37_07E1)

End point description:

Immunogenicity was measured as the percentages of subjects with Anti- PRP concentrations ≥1.0 µg/mL and ≥0.15 µg/mL approximately 4 years after booster vaccination with either Hib-CRM197 or Hib-TT in V37_07E1 trial (2014-005135-13).

Analysis was evaluated on the PPS (i.e. All subjects in the All Enrolled Set with no reportable protocol deviations).

End point type	Secondary

End point timeframe:

At Day 1 (approximately 4 years post booster dose administered in study V37_07E1)

End point values	Hib CRM197	Hib TT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	215	211		
Units: Percentage of subjects				
number (confidence interval 95%)				
Anti-PRP Concentrations ≥ 1.0 µg/mL	77 (71 to 82)	88 (83 to 92)		
Anti-PRP Concentrations ≥ 0.15 µg/mL	77 (71 to 82)	88 (83 to 92)		

Statistical analyses

Statistical analysis title	Anti-PRP Concentrations ≥1.0 µg/mL
Comparison groups	Hib CRM197 v Hib TT
Number of subjects included in analysis	426
Analysis specification	Pre-specified
Analysis type	other
Method	Clopper-Pearson
Parameter estimate	Vaccine Group Differences
Point estimate	-11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-18.6
upper limit	-4.2

Statistical analysis title	Anti-PRP Concentrations ≥0.15 µg/mL
Comparison groups	Hib CRM197 v Hib TT
Number of subjects included in analysis	426
Analysis specification	Pre-specified
Analysis type	other
Method	Clopper-Pearson
Parameter estimate	Vaccine Group Differences
Point estimate	-11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-18.6
upper limit	-4.2

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events:	
NA	
Adverse event reporting additional description:	
Safety was not accessed for this study.	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	NA
Dictionary version	NA

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

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: Safety was not assessed for this study.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported