Clinical trial results:
A phase IV, non-randomised, open-label, multicentre study with two parallel groups to assess the immunogenicity and safety of GlaxoSmithKline (GSK) Biologicals' combined DTPa-HBV-IPV/Hib vaccine administered as a three-dose primary vaccination course at 2, 4 and 6 months of age in healthy infants in Canada.

Summary

EudraCT number	2013-003428-34
Trial protocol	Outside EU/EEA
Global end of trial date	12 March 2013

Results information

Result version number	v1
This version publication date	11 May 2016
First version publication date	30 May 2015

Trial information

Trial identification

Sponsor protocol code	103506

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00753649
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline Biologicals
Sponsor organisation address	Rue de l'Institut 89, Rixensart, Belgium, B-1330
Public contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089904466, GSKClinicalSupportHD@gsk.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	28 November 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 March 2013
Global end of trial reached?	Yes
Global end of trial date	12 March 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the immune response to the Hib component of GSK Biologicals' combined DTPa-HBV-IPV/Hib preservative-free vaccine in terms of seroprotection rates one month after the three-dose primary vaccination course in "Aboriginal infants" and "Other Non-Aboriginal infants".

Protection of trial subjects:

All subjects were supervised after vaccination/product administration with appropriate medical treatment readily available. Vaccines were administered by qualified and trained personnel. Vaccines were administered only to eligible subjects that had no contraindications to any components of the vaccines.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 September 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	Canada: 224
Worldwide total number of subjects	224
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)	224
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

During the screening the following steps occurred: check for inclusion/exclusion criteria, contraindications/precautions, medical history of the subjects and signing informed consent forms.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Infanrix Hexa Aboriginal Group

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Infanrix™ Hexa
Investigational medicinal product code	
Other name	DTPa-HBV-IPV/Hib
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Three doses of Infanrix Hexa™ vaccine were administered by injection, intramuscularly in the right side of the tight, at 2, 4 and 6 months of age.

Investigational medicinal product name	Rotarix™
Investigational medicinal product code	
Other name	HRV
Pharmaceutical forms	Oral drops
Routes of administration	Oral use

Dosage and administration details:

Two doses of Rotarix™ vaccine were administered concomitantly with the first two doses of Infanrix Hexa™ vaccine. Rotarix™ was given orally at 2 and 4 months of age, according to the immunization schedule.

Arm title	Infanrix Hexa Non-Aboriginal Group

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Infanrix™ Hexa
Investigational medicinal product code	
Other name	DTPa-HBV-IPV/Hib
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Three doses of Infanrix Hexa™ vaccine were administered by injection, intramuscularly in the right side of the tight, at 2, 4 and 6 months of age.

Investigational medicinal product name	Rotarix™
Investigational medicinal product code	
Other name	HRV
Pharmaceutical forms	Oral drops

Routes of administration	Oral use

Dosage and administration details:

Two doses of Rotarix™ vaccine were administered concomitantly with the first two doses of Infanrix Hexa™ vaccine. Rotarix™ was given orally at 2 and 4 months of age, according to the immunization schedule.

Number of subjects in period 1	Infanrix Hexa Aboriginal Group	Infanrix Hexa Non-Aboriginal Group
Started	112	112
Completed	105	112
Not completed	7	0
Lost to follow-up (subjects with complete vaccinat	1	-
Protocol Violation	2	-
Lost to follow-up (subjects with incomplete vaccin	3	-
Migrated/moved from study area	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Infanrix Hexa Aboriginal Group
Reporting group description: -	
Reporting group title	Infanrix Hexa Non-Aboriginal Group
Reporting group description: -	

Reporting group values	Infanrix Hexa Aboriginal Group	Infanrix Hexa Non-Aboriginal Group	Total
Number of subjects	112	112	224
Age categorical Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			0
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 65-84 years			0
85 years and over			0
Age continuous Units: weeks			
arithmetic mean	9.3	9.2	
standard deviation	± 1.38	± 1.3	-
Gender categorical Units: Subjects			
Female	62	52	114
Male	50	60	110

End points

End points reporting groups

Reporting group title	Infanrix Hexa Aboriginal Group
Reporting group description: -	
Reporting group title	Infanrix Hexa Non-Aboriginal Group
Reporting group description: -	

Primary: Number of seroprotected subjects against Polyribosyl-ribitol phosphate (anti-PRP)

End point title	Number of seroprotected subjects against Polyribosyl-ribitol phosphate (anti-PRP)[1]
End point description:	
A seroprotected subject was a subject whose anti-PRP antibody concentration was ≥0.15 µg/mL.	
End point type	Primary
End point timeframe:	
One month after (POST) Dose 3.	

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: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	Infanrix Hexa Aboriginal Group	Infanrix Hexa Non-Aboriginal Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	94	107		
Units: Subjects				
Anti-PRP, POST-M1 [N=94,107]	92	106		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-Polyribosyl-ribitol phosphate (anti-PRP) antibodies with concentrations ≥1µg/mL

End point title	Number of subjects with anti-Polyribosyl-ribitol phosphate (anti-PRP) antibodies with concentrations ≥1µg/mL
End point description:	
End point type	Secondary
End point timeframe:	
One month after (POST) Dose 3.	

End point values	Infanrix Hexa Aboriginal Group	Infanrix Hexa Non-Aboriginal Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	94	107		
Units: Subjects				
Anti-PRP, POST-M1 [N=94,107]	83	91		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-PRP antibody concentrations

End point title	Anti-PRP antibody concentrations

End point description:

End point type	Secondary

End point timeframe:

One month after (POST) Dose 3.

End point values	Infanrix Hexa Aboriginal Group	Infanrix Hexa Non-Aboriginal Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	94	107		
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-PRP, POST-M1 [N=94,107]	6.123 (4.498 to 8.334)	3.51 (2.745 to 4.488)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroprotected subjects against Hepatitis B (anti-HBs), with anti-HBs antibody concentrations ≥ 10 µg/mL

End point title	Number of seroprotected subjects against Hepatitis B (anti-HBs), with anti-HBs antibody concentrations ≥ 10 µg/mL

End point description:

End point type	Secondary

End point timeframe:

One month after (POST) Dose 3.

End point values	Infanrix Hexa Aboriginal Group	Infanrix Hexa Non-Aboriginal Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	103		
Units: Subjects				
Anti-HBs, POST-M1 [N=91,103]	91	103		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with Anti-HBs antibody concentrations ≥100 mIU/mL

End point title	Number of subjects with Anti-HBs antibody concentrations ≥100 mIU/mL

End point description:

End point type	Secondary

End point timeframe:

One month after (POST) Dose 3.

End point values	Infanrix Hexa Aboriginal Group	Infanrix Hexa Non-Aboriginal Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	103		
Units: Subjects				
Anti-HBs, POST-M1 [N=91,103]	89	100		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-HBs antibody concentrations

End point title	Anti-HBs antibody concentrations

End point description:

End point type	Secondary

End point timeframe:

One month after (POST) Dose 3.

End point values	Infanrix Hexa Aboriginal Group	Infanrix Hexa Non-Aboriginal Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	103		
Units: mIU/mL				
geometric mean (confidence interval 95%)				
Anti-HBs, POST-M1 [N=91,103]	1797.9 (1375.1 to 2350.7)	1544.4 (1210.4 to 1970.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with unsolicited adverse events (AEs)

End point title	Number of subjects with unsolicited adverse events (AEs)

End point description:

End point type	Secondary

End point timeframe:

During the 31 day (Days 0-30) post vaccination

End point values	Infanrix Hexa Aboriginal Group	Infanrix Hexa Non-Aboriginal Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	112	112		
Units: Subjects				
Any AEs, [N=112.112]	26	19		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with serious adverse events (SAEs)

End point title	Number of subjects with serious adverse events (SAEs)

End point description:

End point type	Secondary

End point timeframe:
During the entire study period

End point values	Infanrix Hexa Aboriginal Group	Infanrix Hexa Non-Aboriginal Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	112	112		
Units: Subjects				
Any SAEs, [N=112.112]	6	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Unsolicited AEs during the 31-day post-vaccination period, SAEs during the entire period

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups

Reporting group title	Infanrix Hexa Aboriginal Group
Reporting group description: -	
Reporting group title	Infanrix Hexa Non-Aboriginal Group

Reporting group description: -

Serious adverse events	Infanrix Hexa Aboriginal Group	Infanrix Hexa Non-Aboriginal Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 112 (5.36%)	0 / 112 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Nervous system disorders			
Convulsion			
subjects affected / exposed	2 / 112 (1.79%)	0 / 112 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile convulsion			
subjects affected / exposed	1 / 112 (0.89%)	0 / 112 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 112 (0.89%)	0 / 112 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bronchiolitis			

subjects affected / exposed	1 / 112 (0.89%)	0 / 112 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia bacterial			
subjects affected / exposed	1 / 112 (0.89%)	0 / 112 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus infection			
subjects affected / exposed	1 / 112 (0.89%)	0 / 112 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Infanrix Hexa Aboriginal Group	Infanrix Hexa Non-Aboriginal Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	26 / 112 (23.21%)	19 / 112 (16.96%)	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	26 / 112 (23.21%)	19 / 112 (16.96%)	
occurrences (all)	26	19	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 June 2010	Amendment 2 The protocol was originally designed for sites in British Columbia (BC) and therefore the vaccines that the subject may receive outside of the study were recommended according to the BC vaccination schedule. New sites were selected in provinces where the recommended schedule for vaccine co-administration is different from BC, therefore the protocol is being amended to allow vaccine coadministration according to the provincial schedule rather than the BC schedules. • Some formatting errors have been corrected in the protocol.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported