Clinical trial results:
Phase III b, open, randomised, multicenter study to evaluate the immunogenicity and safety of GlaxoSmithKline Biologicals' combined diphtheria-tetanus-acellular pertussis-hepatitis B-inactivated polio-conjugated Haemophilus influenzae type b vaccine (Infanrix™ hexa) in Indian infants according to a 6-10-14 week schedule, when compared to Infanrix™ hexa given to Indian infants according to a 2-4-6 month schedule.

Summary

EudraCT number	2012-002426-70
Trial protocol	Outside EU/EEA
Global end of trial date	14 August 2006

Results information

Result version number	v1 (current)
This version publication date	19 April 2016
First version publication date	24 June 2015

Trial information

Trial identification

Sponsor protocol code	104005

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00316147
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 2089-904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089-904466, 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?	Yes
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	16 April 2007
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 August 2006
Global end of trial reached?	Yes
Global end of trial date	14 August 2006
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the antibody response to pertussis toxin (PT), filamentous haemagglutinin (FHA), pertactin (PRN) and poliovirus types 1, 2, 3 after a three-dose primary vaccination course with Infanrix hexa.

Protection of trial subjects:

The vaccines were to be observed closely for at least 30 minutes, with appropriate medical treatment readily available in case of a rare anaphylactic reaction following the administration of vaccines.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 December 2005
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	India: 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 Group A

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Infanrix™ Hexa
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Single dose intramuscular injection in the upper lateral quadrant of the thigh at 6, 10 and 14 weeks of age.

Arm title	Infanrix hexa Group B

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Infanrix™ Hexa
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Single dose intramuscular injection in the upper lateral quadrant of the thigh at 2, 4 and 6 months of age.

Number of subjects in period 1	Infanrix hexa Group A	Infanrix hexa Group B
Started	112	112
Completed	109	107
Not completed	3	5
Consent withdrawn by subject	2	1
Migrated/moved from study area	1	3
Protocol deviation	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Infanrix hexa Group A
Reporting group description: -	
Reporting group title	Infanrix hexa Group B
Reporting group description: -	

Reporting group values	Infanrix hexa Group A	Infanrix hexa Group B	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	6.9	6.8	
standard deviation	± 1.16	± 0.95	-
Gender categorical			
Units: Subjects			
Female	53	53	106
Male	59	59	118

End points

End points reporting groups

Reporting group title	Infanrix hexa Group A
Reporting group description: -	
Reporting group title	Infanrix hexa Group B
Reporting group description: -	

Primary: Vaccine response to anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin (anti-FHA) and anti-pertactin (anti-PRN).

End point title	Vaccine response to anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin (anti-FHA) and anti-pertactin (anti-PRN).[1]

End point description:

Vaccine response was defined as appearance of antibodies following vaccination (i.e., post- vaccination antibody concentration ≥ the assay cut-off) for initially sero-negative subjects. For initially sero-positive subjects, response is defined as post vaccination concentration at least equal to concentration before vaccination (post-vaccination concentration ≥ pre vaccination concentration).
Immunogenicity analyses could not be performed due to inadvertent contamination of blood samples.

End point type	Primary

End point timeframe:

One month after the third dose.

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 Group A	Infanrix hexa Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	112	112		
Units: Subjects				
Anti-PT	0	0		
Anti-FHA	0	0		
Anti-PRN	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any solicited local symptoms.

End point title	Number of subjects reporting any solicited local symptoms.

End point description:

End point type	Secondary

End point timeframe:

During the 4-day (Day 0-3) post-vaccination period.

End point values	Infanrix hexa Group A	Infanrix hexa Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	111	110		
Units: Subjects				
Any Pain, D1	55	46		
Any Redness, D1	24	35		
Any Swelling, D1	29	26		
Any Pain, D2	50	42		
Any Redness, D2	21	29		
Any Swelling, D2	34	31		
Any Pain, D3	38	38		
Any Redness, D3	16	27		
Any Swelling, D3	25	26		
Any Pain, Overall	66	63		
Any Redness, Overall	38	52		
Any Swelling, Overall	47	44		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any solicited general symptoms.

End point title	Number of subjects reporting any solicited general symptoms.

End point description:

End point type	Secondary

End point timeframe:

During the 4-day (Day 0-3) post-vaccination period.

End point values	Infanrix hexa Group A	Infanrix hexa Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	110	110		
Units: Subjects				
Any Drowsiness, D1	19	22		
Any Fever (Axillary), D1	21	20		
Any Irritability, D1	26	31		
Any Loss of appetite, D1	14	13		
Any Drowsiness, D2	14	21		
Any Fever (Axillary), D2	26	27		
Any Irritability, D2	31	28		
Any Loss of appetite, D2	7	15		

Any Drowsiness, D3	9	13		
Any Fever (Axillary), D3	17	23		
Any Irritability, D3	20	28		
Any Loss of appetite, D3	6	13		
Any Drowsiness, Overall	26	36		
Any Fever (Axillary), Overall	51	44		
Any Irritability, Overall	44	48		
Any Loss of appetite, Overall	19	28		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any unsolicited adverse events (AEs).

End point title	Number of subjects reporting any unsolicited adverse events (AEs).

End point description:

End point type	Secondary

End point timeframe:

During the 31-day (Day 0-30) period after vaccination.

End point values	Infanrix hexa Group A	Infanrix hexa Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	112	112		
Units: Subjects				
Any AE(s)	30	18		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any serious adverse events (SAEs).

End point title	Number of subjects reporting any serious adverse events (SAEs).

End point description:

End point type	Secondary

End point timeframe:

During the entire study period.

End point values	Infanrix hexa Group A	Infanrix hexa Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	112	112		
Units: Subjects				
Any SAE(s)	3	3		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Unsolicited local an general symptoms: during the 4-day (Day 0–3) post-vaccination period;
Unsolicited adverse events (AEs): during the 31-day (Day 0-30) period after vaccination;
Serious adverse events (SAEs): During the entire study period.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	9.1

Reporting groups

Reporting group title	Infanrix hexa Group A
Reporting group description: -	
Reporting group title	Infanrix hexa Group B

Reporting group description: -

Serious adverse events	Infanrix hexa Group A	Infanrix hexa Group B	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 112 (2.68%)	6 / 112 (5.36%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Gastrointestinal disorders			
Diarrhea			
subjects affected / exposed	0 / 112 (0.00%)	1 / 112 (0.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Bronchial hyperreactivity			
subjects affected / exposed	0 / 112 (0.00%)	1 / 112 (0.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bronchiolitis			
subjects affected / exposed	1 / 112 (0.89%)	1 / 112 (0.89%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess			

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	
Gastroenteritis			
subjects affected / exposed	0 / 112 (0.00%)	1 / 112 (0.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	0 / 112 (0.00%)	1 / 112 (0.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
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 tract infection			
subjects affected / exposed	0 / 112 (0.00%)	1 / 112 (0.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
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 Group A	Infanrix hexa Group B	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	66 / 112 (58.93%)	63 / 112 (56.25%)	
General disorders and administration site conditions			
Pain			
alternative assessment type: Systematic			
subjects affected / exposed[1]	66 / 111 (59.46%)	63 / 110 (57.27%)	
occurrences (all)	66	63	
Redness			
alternative assessment type: Systematic			

subjects affected / exposed[2]	38 / 111 (34.23%)	52 / 110 (47.27%)	
occurrences (all)	38	52	
Swelling			
alternative assessment type: Systematic			
subjects affected / exposed[3]	47 / 111 (42.34%)	44 / 110 (40.00%)	
occurrences (all)	47	44	
Drowsiness			
alternative assessment type: Systematic			
subjects affected / exposed[4]	26 / 111 (23.42%)	36 / 110 (32.73%)	
occurrences (all)	26	36	
Fever (Axillary)			
alternative assessment type: Systematic			
subjects affected / exposed[5]	51 / 111 (45.95%)	44 / 110 (40.00%)	
occurrences (all)	51	44	
Irritability			
alternative assessment type: Systematic			
subjects affected / exposed[6]	44 / 111 (39.64%)	48 / 110 (43.64%)	
occurrences (all)	44	48	
Loss of appetite			
alternative assessment type: Systematic			
subjects affected / exposed[7]	19 / 111 (17.12%)	28 / 110 (25.45%)	
occurrences (all)	19	28	
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	7 / 112 (6.25%)	7 / 112 (6.25%)	
occurrences (all)	7	7	
Nasopharyngitis			
subjects affected / exposed	8 / 112 (7.14%)	0 / 112 (0.00%)	
occurrences (all)	8	0	

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Solicited local/general symptoms were tabulated only for subjects with a symptom sheet completed.
[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Solicited local/general symptoms were tabulated only for subjects with a symptom sheet completed.

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Solicited local/general symptoms were tabulated only for subjects with a symptom sheet completed.
[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Solicited local/general symptoms were tabulated only for subjects with a symptom sheet completed.
[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Solicited local/general symptoms were tabulated only for subjects with a symptom sheet completed.
[6] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Solicited local/general symptoms were tabulated only for subjects with a symptom sheet completed.
[7] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Solicited local/general symptoms were tabulated only for subjects with a symptom sheet completed.

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