



Clinical trial results:

A phase III, randomized, single-blind, controlled study to assess the immunogenicity, safety and reactogenicity of GlaxoSmithKline (GSK) Biologicals' 10-valent pneumococcal conjugate vaccine as a 3-dose primary immunization course at 6, 10 and 14 weeks of age in India, co-administered with GSK Biologicals' Tritanrix-HepB/Hib (DTPw-HBV/Hib) vaccine.

Summary

EudraCT number	2011-004644-22
Trial protocol	Outside EU/EEA
Global end of trial date	13 November 2009

Results information

Result version number	v1
This version publication date	01 April 2016
First version publication date	23 July 2015

Trial information

Trial identification

Sponsor protocol code	111188
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00814710
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?	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 April 2010
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 November 2009
Global end of trial reached?	Yes
Global end of trial date	13 November 2009
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the immunogenicity of GSK Biologicals' 10-valent pneumococcal conjugate vaccine in India, one month post dose 3.

Protection of trial subjects:

All subjects were supervised closely for at least 30 minutes following vaccination 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. Subjects were followed-up for one month (minimum 30 days) following administration of the last dose of study vaccines.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 March 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	India: 360
Worldwide total number of subjects	360
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)	360
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	Single blind
Roles blinded	Subject

Blinding implementation details:

This study was conducted in a single-blind manner meaning that the investigator and the study staff are aware of the treatment assignment but the subject's parent(s)/guardian(s) are not.

Arms

Are arms mutually exclusive?	Yes
Arm title	Synflorix & Tritanrix-HepB/Hib Group

Arm description:

Subjects received Pneumococcal conjugate vaccine GSK1024850A intramuscularly in the right thigh co-administered with TritanrixTM-HepB/Hib intramuscularly in the left thigh at 6-10-14 weeks of age (=study month 0, 1, 2)

Arm type	Experimental
Investigational medicinal product name	Pneumococcal conjugate vaccine GSK1024850A
Investigational medicinal product code	
Other name	10Pn-PD-DiT
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

3 doses at 6-10-14 weeks of age (=study month 0, 1, 2) administered in the right thigh

Investigational medicinal product name	Tritanrix TM -HepB/Hib
Investigational medicinal product code	
Other name	DTPw-HBV/Hib
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

3 doses at 6-10-14 weeks of age (=study month 0, 1, 2) administered in the left thigh

Arm title	Hiberix group & Tritanrix-HepB Group
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Arm description:

Subjects received HiberixTM intramuscularly in the right thigh co-administered with TritanrixTM-HepB intramuscularly in the left thigh at 6-10-14 weeks of age (=study month 0, 1, 2).

Arm type	Active comparator
Investigational medicinal product name	Hiberix TM
Investigational medicinal product code	
Other name	Hib
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

3 doses at 6-10-14 weeks of age (=study month 0, 1, 2) administered in the right thigh

Investigational medicinal product name	Tritanrix™-HepB
Investigational medicinal product code	
Other name	DTPw-HBV
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

3 doses at 6-10-14 weeks of age (=study month 0, 1, 2) administered in the left thigh

Number of subjects in period 1	Synflorix & Tritanrix-HepB/Hib Group	Hiberix group & Tritanrix-HepB Group
Started	240	120
Completed	232	117
Not completed	8	3
Adverse event, serious fatal	1	-
Lost to follow-up	7	3

Baseline characteristics

Reporting groups

Reporting group title	Synflorix & Tritanrix-HepB/Hib Group
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Reporting group description:

Subjects received Pneumococcal conjugate vaccine GSK1024850A intramuscularly in the right thigh co-administered with TritanrixTM-HepB/Hib intramuscularly in the left thigh at 6-10-14 weeks of age (=study month 0, 1, 2)

Reporting group title	Hiberix group & Tritanrix-HepB Group
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Reporting group description:

Subjects received HiberixTM intramuscularly in the right thigh co-administered with TritanrixTM-HepB intramuscularly in the left thigh at 6-10-14 weeks of age (=study month 0, 1, 2).

Reporting group values	Synflorix & Tritanrix-HepB/Hib Group	Hiberix group & Tritanrix-HepB Group	Total
Number of subjects	240	120	360
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	6.7	6.7	
standard deviation	± 1.08	± 1.05	-
Gender categorical Units: Subjects			
Female	109	66	175
Male	131	54	185

End points

End points reporting groups

Reporting group title	Synflorix & Tritanrix-HepB/Hib Group
Reporting group description: Subjects received Pneumococcal conjugate vaccine GSK1024850A intramuscularly in the right thigh co-administered with TritanrixTM-HepB/Hib intramuscularly in the left thigh at 6-10-14 weeks of age (=study month 0, 1, 2)	
Reporting group title	Hiberix group & Tritanrix-HepB Group
Reporting group description: Subjects received HiberixTM intramuscularly in the right thigh co-administered with TritanrixTM-HepB intramuscularly in the left thigh at 6-10-14 weeks of age (=study month 0, 1, 2).	

Primary: Concentrations of antibodies against vaccine pneumococcal serotypes.

End point title	Concentrations of antibodies against vaccine pneumococcal serotypes. ^[1]
End point description: Antibodies assessed for this outcome measure were those against the vaccine pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F (ANTI-1, -4, -5, -6B, -7F, -9V, -14, -18C, -19F and -23F). Antibody concentrations were measured by 22F enzyme-linked immunosorbent assay (ELISA), expressed as geometric mean concentrations (GMCs), in micrograms per milliliter (µg/mL). The seropositivity cut-off of the assay was an antibody concentration ≥ 0.05 µg/mL	
End point type	Primary
End point timeframe: One month after primary immunization (month 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	Synflorix & Tritanrix-HepB/Hib Group	Hiberix group & Tritanrix-HepB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	229	116		
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-1	3.27 (2.91 to 3.67)	0.03 (0.03 to 0.04)		
Anti-4	3.8 (3.33 to 4.33)	0.04 (0.03 to 0.05)		
Anti-5	4.17 (3.72 to 4.67)	0.05 (0.04 to 0.05)		
Anti-6B	0.71 (0.59 to 0.86)	0.05 (0.04 to 0.06)		
Anti-7F	3.87 (3.47 to 4.31)	0.06 (0.05 to 0.07)		
Anti-9V	4.21 (3.71 to 4.78)	0.06 (0.05 to 0.08)		
Anti-14	5.21 (4.51 to 6.01)	0.26 (0.2 to 0.34)		

Anti-18C	15.23 (12.96 to 17.9)	0.07 (0.05 to 0.08)		
Anti-19F	11.78 (10.26 to 13.53)	0.12 (0.1 to 0.16)		
Anti-23F	1.18 (0.98 to 1.42)	0.05 (0.04 to 0.05)		

Statistical analyses

No statistical analyses for this end point

Primary: Concentration of antibody against protein D (PD).

End point title	Concentration of antibody against protein D (PD). ^[2]
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End point description:

ANTI-PD concentrations are expressed as geometric mean concentrations (GMCs), in enzyme-linked immunosorbent assay (ELISA) unit per milliliter (EL.U/mL). Seropositivity status is defined as Anti-PD antibody concentrations ≥ 100 EL.U/mL.

End point type	Primary
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End point timeframe:

One month after primary immunization (month 3).

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

End point values	Synflorix & Tritanrix-HepB/Hib Group	Hiberix group & Tritanrix-HepB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	227	116		
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PD, M3	2981.7 (2703 to 3289.2)	63.9 (55.8 to 73.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with opsonophagocytic activity against pneumococcal serotypes.

End point title	Number of subjects with opsonophagocytic activity against pneumococcal serotypes.
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End point description:

Vaccine pneumococcal serotypes included 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F. Cross-reactive pneumococcal serotypes included 6A and 19A. Opsonophagocytic activity was defined as the dilution of serum (opsonic titer) able to sustain 50% killing of live pneumococci under the assay conditions. The cut-off of the assay was an opsonic titer equal to or greater than 8.

End point type	Secondary
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End point timeframe:

One month after primary immunization (month 3).

End point values	Synflorix & Tritanrix-HepB/Hib Group	Hiberix group & Tritanrix-HepB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	116	57		
Units: Subjects				
Opsono-1 (N=116; 57)	105	3		
Opsono-4 (N=116; 55)	114	24		
Opsono-5 (N= 116; 56)	111	2		
Opsono-6B (N=116; 54)	98	5		
Opsono-7F (N=116; 53)	116	35		
Opsono-9V (N=115; 56)	113	9		
Opsono-14 (N=115; 56)	110	14		
Opsono-18C (N=115; 55)	113	2		
Opsono-19F (N=116; 56)	114	7		
Opsono-23F (N=116; 54)	113	9		
Opsono-6A (N=110;57)	54	7		
Opsono-19A (N=109;57)	35	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with antibody concentrations against pneumococcal serotypes equal to or above cut-off value.

End point title	Number of subjects with antibody concentrations against pneumococcal serotypes equal to or above cut-off value.
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End point description:

Vaccine pneumococcal serotypes included 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F. Cross-reactive pneumococcal serotypes included 6A and 19A. The cut-off was defined as 0.20 microgram per milliliter (µg/mL).

End point type	Secondary
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End point timeframe:

One month after primary immunization.

End point values	Synflorix & Tritanrix-HepB/Hib Group	Hiberix group & Tritanrix-HepB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	229	116		
Units: Subjects				

Anti-1	228	2		
Anti-4	225	10		
Anti-5	226	10		
Anti-6B	178	9		
Anti-7F	228	16		
Anti-9V	227	21		
Anti-14	229	66		
Anti-18C	227	20		
Anti-19F	227	40		
Anti-23F	205	12		
Anti-6A (N=229;115)	95	12		
Anti-19A	146	21		

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of antibodies against pneumococcal cross-reactive serotypes.

End point title	Concentrations of antibodies against pneumococcal cross-reactive serotypes.
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End point description:

Antibodies assessed for this outcome measure were those against the vaccine pneumococcal cross-reactive serotypes 6A and 19A (ANTI6A and -19A). Antibody concentrations were measured by 22F enzyme-linked immunosorbent assay (ELISA), expressed as geometric mean concentrations (GMCs), in micrograms per milliliter (µg/mL). The seropositivity cut-off of the assay was an antibody concentration ≥ 0.05 µg/mL

End point type	Secondary
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End point timeframe:

One month after primary immunization (month 3).

End point values	Synflorix & Tritanrix-HepB/Hib Group	Hiberix group & Tritanrix-HepB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	229	116		
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-6A (N=229;115)	0.15 (0.13 to 0.18)	0.06 (0.05 to 0.08)		
Anti-19A	0.33 (0.27 to 0.39)	0.08 (0.06 to 0.09)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seropositive for pneumococcal serotypes.

End point title	Number of subjects seropositive for pneumococcal serotypes.
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End point description:

Vaccine pneumococcal serotypes included 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F. Cross-reactive pneumococcal serotypes included 6A and 19A. Seropositivity was defined as a titer equal to or greater than 0.05 µg/mL.

End point type	Secondary
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End point timeframe:

One month after primary immunization (month 3).

End point values	Synflorix & Tritanrix-HepB/Hib Group	Hiberix group & Tritanrix-HepB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	229	116		
Units: Subjects				
Anti-1	228	19		
Anti-4	228	24		
Anti-5	229	46		
Anti-6B	215	40		
Anti-7F	229	52		
Anti-9V	228	49		
Anti-14	229	101		
Anti-18C	227	56		
Anti-19F	229	90		
Anti-23F	220	37		
Anti-6A (N=229;115)	188	62		
Anti-19A	207	71		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seropositive for protein D (PD).

End point title	Number of subjects seropositive for protein D (PD).
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End point description:

Seropositivity for PD was defined greater than or equal to 100 EL.U/mL.

End point type	Secondary
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End point timeframe:

One month after primary immunization (month 3).

End point values	Synflorix & Tritanrix-HepB/Hib Group	Hiberix group & Tritanrix-HepB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	227	116		
Units: Subjects				
Anti-PD, M3	226	16		

Statistical analyses

No statistical analyses for this end point

Secondary: Concentration of antibody against polyribosyl-ribitol phosphate (PRP).

End point title	Concentration of antibody against polyribosyl-ribitol phosphate (PRP).
End point description: Concentration is expressed as GMC in µg/mL. Seroprotection status, defined as Anti-PRP antibody concentration equal to or greater than 0.15 µg/mL.	
End point type	Secondary
End point timeframe: One month after primary immunization (month 3).	

End point values	Synflorix & Tritanrix-HepB/Hib Group	Hiberix group & Tritanrix-HepB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	113	116		
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-PRP	31.367 (26.417 to 37.246)	34.415 (26.847 to 44.116)		

Statistical analyses

No statistical analyses for this end point

Secondary: Concentration of antibodies against diphteria (anti-DT) and tetanus (anti-TT).

End point title	Concentration of antibodies against diphteria (anti-DT) and tetanus (anti-TT).
End point description: Concentrations were expressed as GMCs in International Units per milliliter (IU/mL). Seroprotection status, defined as Anti-DT or Anti-TT antibody concentration equal to or greater than 0.1 IU/mL.	
End point type	Secondary

End point timeframe:

One month after primary immunization (month 3).

End point values	Synflorix & Tritanrix-HepB/Hib Group	Hiberix group & Tritanrix-HepB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	113	116		
Units: IU/mL				
geometric mean (confidence interval 95%)				
Anti-DT	2.58 (2.146 to 3.102)	2.065 (1.736 to 2.457)		
Anti-TT	3.726 (3.182 to 4.363)	1.542 (1.316 to 1.807)		

Statistical analyses

No statistical analyses for this end point

Secondary: Concentration of antibody against Bordetella pertussis (BPT).

End point title	Concentration of antibody against Bordetella pertussis (BPT).
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End point description:

Concentration was expressed as GMC in EL.U/mL. Seropositivity status, defined as Anti-BPT antibody concentration equal to or greater than 15 EL.U/mL

End point type	Secondary
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End point timeframe:

One month after primary immunization (month 3).

End point values	Synflorix & Tritanrix-HepB/Hib Group	Hiberix group & Tritanrix-HepB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	113	116		
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-BPT	90.3 (80.3 to 101.6)	114.5 (101.2 to 129.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Concentration of antibody against hepatitis B (anti-HBs) by Enzyme-Linked ImmunoSorbent Assay (ELISA).

End point title	Concentration of antibody against hepatitis B (anti-HBs) by Enzyme-Linked ImmunoSorbent Assay (ELISA).
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End point description:

Concentration was expressed as GMC in milli international units per milliliter (mIU/mL). As a decrease in the specificity of the anti-HBs ELISA assay had been observed in some studies for low levels of antibody (10-100 mIU/mL), the table shows results following partial or complete retesting/reanalysis.

End point type	Secondary
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End point timeframe:

One month after primary immunization (month 3).

End point values	Synflorix & Tritanrix-HepB/Hib Group	Hiberix group & Tritanrix-HepB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	92	89		
Units: mIU/mL				
geometric mean (confidence interval 95%)				
Anti-HBS	1970.5 (1614.9 to 2404.5)	1378.2 (1115.6 to 1702.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seropositive for B. pertussis (BPT)

End point title	Number of subjects seropositive for B. pertussis (BPT)
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End point description:

Seropositivity was defined as and antibody concentration equal to or greater than 15 EL.U/mL.

End point type	Secondary
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End point timeframe:

One month after primary immunization (month 3).

End point values	Synflorix & Tritanrix-HepB/Hib Group	Hiberix group & Tritanrix-HepB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	113	116		
Units: Subjects				
Anti-BPT	113	116		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroprotected subjects (anti-DT, anti-TT, anti-PRP, anti-HBs).

End point title	Number of seroprotected subjects (anti-DT, anti-TT, anti-PRP, anti-HBs).
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End point description:

Seroprotection was defined as: Anti-DT antibody concentration equal to or greater than 0.1 IU/mL. Anti-TT antibody concentration equal to or greater than 0.1 IU/mL. Anti-PRP antibody concentration equal to or greater than 0.15 µg/mL Anti-HBs antibody concentration greater than or equal to 10 mIU/mL.

End point type	Secondary
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End point timeframe:

One month after primary immunization (month 3).

End point values	Synflorix & Tritanrix-HepB/Hib Group	Hiberix group & Tritanrix-HepB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	113	116		
Units: Subjects				
Anti-DT	113	116		
Anti-TT	113	116		
Anti-PRP 0.15	113	116		
Anti-HBs (N=92,89)	92	89		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroprotected subjects (anti-PRP above the cut-off of 1.0 µg/mL).

End point title	Number of seroprotected subjects (anti-PRP above the cut-off of 1.0 µg/mL).
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End point description:

Anti-PRP antibody concentration equal to or greater than 1.0 µg/mL.

End point type	Secondary
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End point timeframe:

One month after primary immunization (month 3).

End point values	Synflorix & Tritanrix-HepB/Hib Group	Hiberix group & Tritanrix-HepB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	113	116		
Units: Subjects				
Anti-PRP	113	114		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with solicited local symptoms (any and grade 3).

End point title	Number of subjects with solicited local symptoms (any and grade 3).
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End point description:

Solicited local symptoms included pain, redness and swelling. Any = Occurrence of the local symptom, regardless of intensity. Grade 3 Pain = Crying when limb was moved/spontaneously painful. Grade 3 Redness/Swelling = at injection site larger than (>) 30 millimeters (mm).

End point type	Secondary
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End point timeframe:

Within 4 days (day 0-3) after each vaccination.

End point values	Synflorix & Tritanrix-HepB/Hib Group	Hiberix group & Tritanrix-HepB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	238	119		
Units: Subjects				
Any Pain dose 1 (N=238,119)	188	93		
Grade 3 Pain dose 1 (N=238,119)	85	33		
Any Redness dose 1 (N=238,119)	82	52		
Grade 3 Redness dose 1 (N=238,119)	6	1		
Any Swelling dose 1 (N=238,119)	125	70		
Grade 3 Swelling dose 1 (N=238,119)	31	16		
Any Pain dose 2 (N=237,118)	167	83		
Grade 3 Pain dose 2 (N=237,118)	57	25		
Any Redness dose 2 (N=237,118)	75	39		
Grade 3 Redness dose 2 (N=237,118)	2	0		
Any Swelling dose 2 (N=237,118)	107	51		
Grade 3 Swelling dose 2 (N=237,118)	14	9		
Any Pain dose 3 (N=233,117)	148	74		
Grade 3 Pain dose 3 (N=233,117)	54	30		

Any Redness dose 3 (N=233,117)	75	38		
Grade 3 Redness dose 3 (N=233,117)	1	2		
Any Swelling dose 3 (N=233,117)	104	48		
Grade 3 Swelling dose 3 (N=233,117)	15	6		

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).
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End point description:

An AE is any untoward medical occurrence in a clinical investigation subject, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. Unsolicited AE covers any AE reported in addition to those solicited during the clinical study and any solicited symptom with onset outside the specified period of follow-up for solicited symptoms.

End point type	Secondary
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End point timeframe:

Within 31 days (day 0-30) after vaccination.

End point values	Synflorix & Tritanrix-HepB/Hib Group	Hiberix group & Tritanrix-HepB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	240	120		
Units: Subjects				
Any AE(s)	38	17		

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).
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End point description:

SAEs assessed include medical occurrences that result in death, are life threatening, require hospitalization or prolongation of hospitalization, result in disability/incapacity or are a congenital anomaly/birth defect in the offspring of a study subject.

End point type	Secondary
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End point timeframe:

Following first vaccination (Month 0) throughout the entire study period (month 3).

End point values	Synflorix & Tritanrix-HepB/Hib Group	Hiberix group & Tritanrix-HepB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	240	120		
Units: Subjects				
Any SAE(s)	5	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number/percentage of subjects with any and grade 3 solicited general symptoms

End point title	Number/percentage of subjects with any and grade 3 solicited general symptoms
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End point description:

Assessed solicited general symptoms were Drowsiness, Irritability/Fussiness (Irr./Fuss.), Loss of appetite (Loss Appet.) and Fever (rectal temperature higher than [\geq] 38.0 and $>$ 39.0 degrees Celsius [$^{\circ}$ C]),. Any = Occurrence of the specified solicited general symptom, regardless of intensity or relationship to vaccination. Grade 3 Drowsiness = Drowsiness that prevented normal everyday activities. Grade 3 Irr./Fuss. = Crying that could not be comforted/prevented normal everyday activities. Grade 3 Loss of appetite = Subject did not eat at all. Grade 3 Fever = Rectal temperature higher than ($>$) 40.0 $^{\circ}$ C

End point type	Secondary
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End point timeframe:

Within 4 days (day 0-3) after each vaccination

End point values	Synflorix & Tritanrix-HepB/Hib Group	Hiberix group & Tritanrix-HepB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	238	119		
Units: Subjects				
Any Drowsiness dose 1 (N=238,119)	53	26		
Grade 3 Drowsiness dose 1 (N=238,119)	7	4		
Fever \geq 38 $^{\circ}$ C dose 1 (N=238,119)	140	63		
Fever $>$ 39 $^{\circ}$ C dose 1 (N=238,119)	11	2		
Fever $>$ 40 $^{\circ}$ C dose 1 (N=238,119)	1	0		
Any Irritability dose 1 (N=238,119)	142	74		
Grade 3 Irritability dose 1 (N=238,119)	13	6		
Any Loss Appet. dose 1 (N=238,119)	63	31		
Grade 3 Loss Appet. dose 1 (N=238,119)	3	0		
Any Drowsiness dose 2 (N=237,118)	42	22		
Grade 3 Drowsiness dose 2 (N=237,118)	8	4		
Fever \geq 38 $^{\circ}$ C dose 2 (N=237,118)	108	43		

Fever >39°C dose 2 (N=237,118)	7	1		
Fever >40°C dose 2 (N=237,118)	0	0		
Any Irritability dose 2 (N=237,118)	123	54		
Grade 3 Irritability dose 2 (N=237,118)	26	5		
Any Loss Appet. dose 2 (N=237,118)	57	27		
Grade 3 Loss Appet. dose 2 (N=237,118)	3	0		
Any Drowsiness dose 3 (N=233,117)	37	15		
Grade 3 Drowsiness dose 3 (N=233,117)	8	1		
Fever ≥38°C dose 3 (N=233,117)	96	31		
Fever >39°C dose 3 (N=233,117)	8	2		
Fever >40°C dose 3 (N=233,117)	2	0		
Any Irritability dose 3 (N=233,117)	109	46		
Grade 3 Irritability dose 3 (N=233,117)	20	4		
Any Loss Appet. dose 3 (N=233,117)	49	20		
Grade 3 Loss Appet. dose 3 (N=233,117)	3	2		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

For other AEs day 0-3 (solicited) and day 0-30 unsolicited. For SAEs month 0 to Month 3.

Adverse event reporting additional description:

The occurrence of reported AEs (all/related) was not available and is encoded as equal to the number of subjects affected.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	12.1
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Reporting groups

Reporting group title	Synflorix and Tritanrix-HepB/Hib Group
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Reporting group description:

Subjects received SynflorixTM (GSK1024850A) intramuscularly in the right thigh co-administered with TritanrixTM-HepB/Hib intramuscularly in the left thigh at 6-10-14 weeks of age (=study month 0, 1, 2).

Reporting group title	Hiberix group and Tritanrix-HepB Group
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Reporting group description:

Subjects received HiberixTM intramuscularly in the right thigh co-administered with TritanrixTM-HepB intramuscularly in the left thigh at 6-10-14 weeks of age (=study month 0, 1, 2)

Serious adverse events	Synflorix and Tritanrix-HepB/Hib Group	Hiberix group and Tritanrix-HepB Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 240 (2.08%)	1 / 120 (0.83%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events	0	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 240 (1.25%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypochromic anaemia			
subjects affected / exposed	1 / 240 (0.42%)	0 / 120 (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 / 240 (0.42%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pneumonia aspiration			
subjects affected / exposed	1 / 240 (0.42%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Infections and infestations			
Bronchopneumonia			
subjects affected / exposed	2 / 240 (0.83%)	1 / 120 (0.83%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chikungunya virus infection			
subjects affected / exposed	1 / 240 (0.42%)	0 / 120 (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	1 / 240 (0.42%)	0 / 120 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	1 / 240 (0.42%)	0 / 120 (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	Synflorix and Tritanrix-HepB/Hib Group	Hiberix group and Tritanrix-HepB Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	209 / 240 (87.08%)	105 / 120 (87.50%)	
General disorders and administration site conditions			

Pain			
alternative assessment type: Systematic			
subjects affected / exposed ^[1]	209 / 238 (87.82%)	105 / 119 (88.24%)	
occurrences (all)	209	105	
Redness			
alternative assessment type: Systematic			
subjects affected / exposed ^[2]	128 / 238 (53.78%)	76 / 119 (63.87%)	
occurrences (all)	128	76	
Swelling			
alternative assessment type: Systematic			
subjects affected / exposed ^[3]	166 / 238 (69.75%)	83 / 119 (69.75%)	
occurrences (all)	166	83	
Drowsiness			
alternative assessment type: Systematic			
subjects affected / exposed ^[4]	73 / 238 (30.67%)	34 / 119 (28.57%)	
occurrences (all)	73	34	
Fever			
alternative assessment type: Systematic			
subjects affected / exposed ^[5]	182 / 238 (76.47%)	85 / 119 (71.43%)	
occurrences (all)	182	85	
Irritability			
alternative assessment type: Systematic			
subjects affected / exposed ^[6]	178 / 238 (74.79%)	88 / 119 (73.95%)	
occurrences (all)	178	88	
Loss of appetite			
alternative assessment type: Systematic			
subjects affected / exposed ^[7]	96 / 238 (40.34%)	49 / 119 (41.18%)	
occurrences (all)	96	49	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	13 / 240 (5.42%)	4 / 120 (3.33%)	
occurrences (all)	13	4	
Infections and infestations			

Rhinitis			
subjects affected / exposed	13 / 240 (5.42%)	6 / 120 (5.00%)	
occurrences (all)	13	6	
Pyrexia			
subjects affected / exposed	12 / 240 (5.00%)	3 / 120 (2.50%)	
occurrences (all)	12	3	

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: The analysis of the solicited symptom included only subjects with documented data.

[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: The analysis of the solicited symptom included only subjects with documented data.

[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: The analysis of the solicited symptom included only subjects with documented data.

[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: The analysis of the solicited symptom included only subjects with documented data.

[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: The analysis of the solicited symptom included only subjects with documented data.

[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: The analysis of the solicited symptom included only subjects with documented data.

[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: The analysis of the solicited symptom included only subjects with documented data.

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