Clinical trial results:
A phase III, randomized, controlled, single-blind study to evaluate the non-inferiority of GlaxoSmithKline Biologicals' 10-valent pneumococcal conjugate vaccine compared to the 7-valent pneumococcal conjugate vaccine Prevenar™ when administered as a 3-dose primary immunization course at 2, 4 and 6 months of age, co-administered with GSK Biologicals' Hiberix™ vaccine.

Summary

EudraCT number	2015-001505-14
Trial protocol	Outside EU/EEA
Global end of trial date	08 May 2009

Results information

Result version number	v1
This version publication date	01 April 2016
First version publication date	25 July 2015

Trial information

Trial identification

Sponsor protocol code	110808

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00680914
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, 44 2089904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 44 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	31 August 2009
Is this the analysis of the primary completion data?	Yes
Primary completion date	08 May 2009
Global end of trial reached?	Yes
Global end of trial date	08 May 2009
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate that GSK Biologicals' 10-valent pneumococcal conjugate vaccine administered as a three-dose primary vac-cination course in Korea is non-inferior to Prevenar for the immune response against at least 7 of the pneumococcal serotypes contained in the 10-valent pneumococcal conjugate vaccine.

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	10 June 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	Korea, Republic of: 503
Worldwide total number of subjects	503
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)	503
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 Period (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/or his staff were aware of the treatment assignment but the subjects parent(s)/guardian(s) were not.

Arms

Are arms mutually exclusive?	Yes
Arm title	Synflorix Group

Arm description:

Subjects received 3 doses of Synflorix vaccine co-administered with Hiberix vaccine at Study Months 0, 2 and 4.

Arm type	Experimental
Investigational medicinal product name	Pneumococcal vaccine GSK1024850A (Synflorix)
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 administered intramuscularly.

Investigational medicinal product name	GSK Biologicals' Hiberix™
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 administered intramuscularly.

Arm title	Prevenar Group

Arm description:

Subjects received 3 doses of Prevenar vaccine co-administered with Hiberix vaccine at Study Months 0, 2 and 4.

Arm type	Active comparator
Investigational medicinal product name	GSK Biologicals' Hiberix™
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 administered intramuscularly.

Investigational medicinal product name	Prevenar
Investigational medicinal product code	
Other name	7Pn
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

3 doses administered intramuscularly.

Number of subjects in period 1	Synflorix Group	Prevenar Group
Started	374	129
Completed	364	125
Not completed	10	4
Adverse event, serious fatal	-	1
Consent withdrawn by subject	6	3
Lost to follow-up	4	-

Baseline characteristics

Reporting groups	
Reporting group title	Synflorix Group
Reporting group description:	
Subjects received 3 doses of Synflorix vaccine co-administered with Hiberix vaccine at Study Months 0, 2 and 4.	
Reporting group title	Prevenar Group
Reporting group description:	
Subjects received 3 doses of Prevenar vaccine co-administered with Hiberix vaccine at Study Months 0, 2 and 4.	

Reporting group values	Synflorix Group	Prevenar Group	Total
Number of subjects	374	129	503
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	9.5	9.5	
standard deviation	± 1.49	± 1.43	-
Gender categorical			
Units: Subjects			
Female	189	71	260
Male	185	58	243

End points

End points reporting groups

Reporting group title	Synflorix Group
Reporting group description:	
Subjects received 3 doses of Synflorix vaccine co-administered with Hiberix vaccine at Study Months 0, 2 and 4.	
Reporting group title	Prevenar Group
Reporting group description:	
Subjects received 3 doses of Prevenar vaccine co-administered with Hiberix vaccine at Study Months 0, 2 and 4.	

Primary: Number of Subjects With Vaccine Pneumococcal Serotypes Antibody Concentrations Above the Cut-Off Value

End point title	Number of Subjects With Vaccine Pneumococcal Serotypes Antibody Concentrations Above the Cut-Off Value
End point description:	
Anti-pneumococcal antibody cut-off value assessed was 0.20 microgram per milliliter (ug/mL). The vaccine pneumococcal serotypes assessed include 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F, and 23F.	
End point type	Primary
End point timeframe:	
One month after administration of 3rd dose of the pneumococcal conjugate vaccine	

End point values	Synflorix Group	Prevenar Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	344	123		
Units: Subjects				
Anti-1	344	7		
Anti-4	343	123		
Anti-5	344	18		
Anti-6B	318	121		
Anti-7F	344	4		
Anti-9V	343	122		
Anti-14	342	123		
Anti-18C	343	123		
Anti-19F	340	123		
Anti-23F	331	121		

Statistical analyses

Statistical analysis title	Immune response non-inferiority–Anti-4
Statistical analysis description:	
To demonstrate that GSK 1024850A vaccine administered as a three-dose primary vaccination course in Korea is non-inferior to Prevenar™ vaccine for the immune response against at least 7 of the	

pneumococcal serotypes contained in the GSK 1024850A vaccine.

Comparison groups	Synflorix Group v Prevenar Group
Number of subjects included in analysis	467
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Parameter estimate	Difference in percentage
Point estimate	0.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.21
upper limit	1.81

Notes:

[1] - For each of the Prevenar™ vaccine serotypes, non-inferiority was demonstrated if the upper limit of the 2-sided 96.5% confidence interval (CI) (adjusted 1-sided alpha = 0.0175) of the difference between groups (Prevenar Group minus Synflorix Group), in terms of percentage of subjects with pneumococcal antibody concentrations ≥0.2 mg/mL, was lower than 10%.

Statistical analysis title	Immune response non-inferiority –Anti-6B

Statistical analysis description:

To demonstrate that GSK 1024850A vaccine administered as a three-dose primary vaccination course in Korea is non-inferior to Prevenar™ vaccine for the immune response against at least 7 of the pneumococcal serotypes contained in the GSK 1024850A vaccine.

Comparison groups	Synflorix Group v Prevenar Group
Number of subjects included in analysis	467
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
Parameter estimate	Difference in percentage
Point estimate	5.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.92
upper limit	9.86

Notes:

[2] - For each of the Prevenar™ vaccine serotypes, non-inferiority was demonstrated if the upper limit of the 2-sided 96.5% confidence interval (CI) (adjusted 1-sided alpha = 0.0175) of the difference between groups (Prevenar Group minus Synflorix Group), in terms of percentage of subjects with pneumococcal antibody concentrations ≥0.2 mg/mL, was lower than 10%.

Statistical analysis title	Immune response non-inferiority –Anti-9V

Statistical analysis description:

To demonstrate that GSK 1024850A vaccine administered as a three-dose primary vaccination course in Korea is non-inferior to Prevenar™ vaccine for the immune response against at least 7 of the pneumococcal serotypes contained in the GSK 1024850A vaccine.

Comparison groups	Synflorix Group v Prevenar Group
Number of subjects included in analysis	467
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
Parameter estimate	Difference in percentage
Point estimate	-0.52

Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.66
upper limit	1.1

Notes:

[3] - For each of the Prevenar™ vaccine serotypes, non-inferiority was demonstrated if the upper limit of the 2-sided 96.5% confidence interval (CI) (adjusted 1-sided alpha = 0.0175) of the difference between groups (Prevenar Group minus Synflorix Group), in terms of percentage of subjects with pneumococcal antibody concentrations ≥0.2 mg/mL, was lower than 10%.

Statistical analysis title	Immune response non-inferiority –Anti-14

Statistical analysis description:

To demonstrate that GSK 1024850A vaccine administered as a three-dose primary vaccination course in Korea is non-inferior to Prevenar™ vaccine for the immune response against at least 7 of the pneumococcal serotypes contained in the GSK 1024850A vaccine.

Comparison groups	Synflorix Group v Prevenar Group
Number of subjects included in analysis	467
Analysis specification	Pre-specified
Analysis type	non-inferiority[4]
Parameter estimate	Difference in percentage
Point estimate	0.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.92
upper limit	2.28

Notes:

[4] - For each of the Prevenar™ vaccine serotypes, non-inferiority was demonstrated if the upper limit of the 2-sided 96.5% confidence interval (CI) (adjusted 1-sided alpha = 0.0175) of the difference between groups (Prevenar Group minus Synflorix Group), in terms of percentage of subjects with pneumococcal antibody concentrations ≥0.2 mg/mL, was lower than 10%.

Statistical analysis title	Immune response non-inferiority –Anti-18C

Statistical analysis description:

To demonstrate that GSK 1024850A vaccine administered as a three-dose primary vaccination course in Korea is non-inferior to Prevenar™ vaccine for the immune response against at least 7 of the pneumococcal serotypes contained in the GSK 1024850A vaccine.

Comparison groups	Synflorix Group v Prevenar Group
Number of subjects included in analysis	467
Analysis specification	Pre-specified
Analysis type	non-inferiority[5]
Parameter estimate	Difference in percentage
Point estimate	0.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.21
upper limit	1.81

Notes:

[5] - For each of the Prevenar™ vaccine serotypes, non-inferiority was demonstrated if the upper limit of the 2-sided 96.5% confidence interval (CI) (adjusted 1-sided alpha = 0.0175) of the difference between groups (Prevenar Group minus Synflorix Group), in terms of percentage of subjects with pneumococcal antibody concentrations ≥0.2 mg/mL, was lower than 10%.

Statistical analysis title	Immune response non-inferiority –Anti-19F

Statistical analysis description:

To demonstrate that GSK 1024850A vaccine administered as a three-dose primary vaccination course in Korea is non-inferior to Prevenar™ vaccine for the immune response against at least 7 of the pneumococcal serotypes contained in the GSK 1024850A vaccine.

Comparison groups	Synflorix Group v Prevenar Group
Number of subjects included in analysis	467
Analysis specification	Pre-specified
Analysis type	non-inferiority[6]
Parameter estimate	Difference in percentage
Point estimate	1.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.34
upper limit	3.15

Notes:

[6] - For each of the Prevenar™ vaccine serotypes, non-inferiority was demonstrated if the upper limit of the 2-sided 96.5% confidence interval (CI) (adjusted 1-sided alpha = 0.0175) of the difference between groups (Prevenar Group minus Synflorix Group), in terms of percentage of subjects with pneumococcal antibody concentrations ≥0.2 mg/mL, was lower than 10%.

Statistical analysis title	Immune response non-inferiority –Anti-23F

Statistical analysis description:

To demonstrate that GSK 1024850A vaccine administered as a three-dose primary vaccination course in Korea is non-inferior to Prevenar™ vaccine for the immune response against at least 7 of the pneumococcal serotypes contained in the GSK 1024850A vaccine.

Comparison groups	Synflorix Group v Prevenar Group
Number of subjects included in analysis	467
Analysis specification	Pre-specified
Analysis type	non-inferiority[7]
Parameter estimate	Difference in percentage
Point estimate	2.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.65
upper limit	5.34

Notes:

[7] - For each of the Prevenar™ vaccine serotypes, non-inferiority was demonstrated if the upper limit of the 2-sided 96.5% confidence interval (CI) (adjusted 1-sided alpha = 0.0175) of the difference between groups (Prevenar Group minus Synflorix Group), in terms of percentage of subjects with pneumococcal antibody concentrations ≥0.2 mg/mL, was lower than 10%.

Statistical analysis title	Immune response non-inferiority –Anti-1

Statistical analysis description:

To demonstrate that GSK 1024850A vaccine administered as a three-dose primary vaccination course in Korea is non-inferior to Prevenar™ vaccine for the immune response against at least 7 of the pneumococcal serotypes contained in the GSK 1024850A vaccine.

Comparison groups	Synflorix Group v Prevenar Group
Number of subjects included in analysis	467
Analysis specification	Pre-specified
Analysis type	non-inferiority[8]
Parameter estimate	Difference in percentage
Point estimate	-0.58

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.95
upper limit	0.18

Notes:

[8] - For each of the 3 non-Prevenar™ vaccine serotypes (i.e., 1, 5 and 7F), non-inferiority was demonstrated if the upper limit of the 96.5% CI of the difference between the aggregate response for the Prevenar™ vaccine serotypes and responses to 1, 5 and 7F in Synflorix Group, (Aggregate 7Pn [=number of subjects in the Prevenar Group, multiplied by 7] minus Synflorix Group), in terms of percentage of subjects with pneumococcal antibody concentrations ≥ 0.2 mg/mL, was lower than 10%.

Statistical analysis title	Immune response non-inferiority –Anti-5

Statistical analysis description:

To demonstrate that GSK 1024850A vaccine administered as a three-dose primary vaccination course in Korea is non-inferior to Prevenar™ vaccine for the immune response against at least 7 of the pneumococcal serotypes contained in the GSK 1024850A vaccine.

Comparison groups	Synflorix Group v Prevenar Group
Number of subjects included in analysis	467
Analysis specification	Pre-specified
Analysis type	non-inferiority[9]
Parameter estimate	Difference in percentage
Point estimate	-0.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.95
upper limit	0.18

Notes:

[9] - For each of the 3 non-Prevenar™ vaccine serotypes (i.e., 1, 5 and 7F), non-inferiority was demonstrated if the upper limit of the 96.5% CI of the difference between the aggregate response for the Prevenar™ vaccine serotypes and responses to 1, 5 and 7F in Synflorix Group, (Aggregate 7Pn [=number of subjects in the Prevenar Group, multiplied by 7] minus Synflorix Group), in terms of percentage of subjects with pneumococcal antibody concentrations ≥ 0.2 mg/mL, was lower than 10%.

Statistical analysis title	Immune response non-inferiority –Anti-7F

Statistical analysis description:

To demonstrate that GSK 1024850A vaccine administered as a three-dose primary vaccination course in Korea is non-inferior to Prevenar™ vaccine for the immune response against at least 7 of the pneumococcal serotypes contained in the GSK 1024850A vaccine.

Comparison groups	Synflorix Group v Prevenar Group
Number of subjects included in analysis	467
Analysis specification	Pre-specified
Analysis type	non-inferiority[10]
Parameter estimate	Difference in percentage
Point estimate	-0.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.95
upper limit	0.18

Notes:

[10] - For each of the 3 non-Prevenar™ vaccine serotypes (i.e., 1, 5 and 7F), non-inferiority was demonstrated if the upper limit of the 96.5% CI of the difference between the aggregate response for the Prevenar™ vaccine serotypes and responses to 1, 5 and 7F in Synflorix Group, (Aggregate 7Pn [=number of subjects in the Prevenar Group, multiplied by 7] minus Synflorix Group), in terms of percentage of subjects with pneumococcal antibody concentrations ≥ 0.2 mg/mL, was lower than 10%.

Secondary: Number of subjects with a seropositivity status against protein D and defined pneumococcal serotypes

End point title	Number of subjects with a seropositivity status against protein D and defined pneumococcal serotypes

End point description:

Seropositivity status for protein D is defined as anti protein D (anti-PD) antibody concentrations >= 100 Enzyme-Linked Immuno Sorbent Assay (EL) units EL.U/mL. Seropositivity status for pneumococcal serotypes is defined as anti-pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F antibody concentrations >= 0.05 ug/mL.

End point type	Secondary

End point timeframe:

One month after the administration of the 3rd vaccine dose of the pneumococcal conjugate vaccine

End point values	Synflorix Group	Prevenar Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	344	123		
Units: Subjects				
Anti-PD	343	123		
Anti-1	344	44		
Anti-4	344	123		
Anti-5	344	85		
Anti-6B	337	122		
Anti-7F	344	22		
Anti-9V	343	123		
Anti-14	344	123		
Anti-18C	344	123		
Anti-19F	344	123		
Anti-23F	340	122		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with opsonophagocytic activity against pneumococcal serotypes contained in the vaccine above the cut-off value

End point title	Number of subjects with opsonophagocytic activity against pneumococcal serotypes contained in the vaccine above the cut-off value

End point description:

The results were presented as the dilution of serum (opsonic titer) able to sustain 50% killing of live pneumococci under the assay conditions. In this assay the cut-off value for opsonophagocytic activity against pneumococcal antibody assessed was >= 8. The vaccine pneumococcal serotypes assessed include 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F.

End point type	Secondary

End point timeframe:

One month after the administration of the 3rd vaccine dose of the pneumococcal conjugate vaccine

End point values	Synflorix Group	Prevenar Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	165	63		
Units: Subjects				
Opsono-1 (N=162; 62)	150	8		
Opsono-4 (N=161; 63)	158	63		
Opsono-5 (N=165; 62)	161	6		
Opsono-6B (N=162; 63)	152	63		
Opsono-7F (N=164; 59)	164	40		
Opsono-9V (N= 165; 63)	164	62		
Opsono-14 (N= 165; 63)	163	62		
Opsono-18C (N= 159; 63)	142	61		
Opsono-19F (N=164; 61)	159	55		
Opsono-23F (N= 164; 63)	160	62		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With cross-reactive Pneumococcal Serotype Antibody Concentrations Above the Cut-Off Value

End point title	Number of Subjects With cross-reactive Pneumococcal Serotype Antibody Concentrations Above the Cut-Off Value

End point description:

Anti-pneumococcal antibody cut-off value assessed was 0.20 microgram per milliliter (ug/mL). Pneumococcal cross-reactive serotypes were 6A and 19A.

End point type	Secondary

End point timeframe:

One month after the administration of the 3rd vaccine dose of the pneumococcal conjugate vaccine

End point values	Synflorix Group	Prevenar Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	344	123		
Units: Subjects				
Anti-6A	232	85		
Anti-19A	203	33		

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations against Pneumococal serotypes contained in the vaccine

End point title	Antibody concentrations against Pneumococal serotypes contained in the vaccine

End point description:

Concentrations are reported as Geometric Mean Concentrations in ug/mL. Pneumococcal serotypes assessed include 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F, and 23F.

End point type	Secondary

End point timeframe:

One month after the administration of the 3rd vaccine dose of the pneumococcal conjugate vaccine

End point values	Synflorix Group	Prevenar Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	344	123		
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-1	3.41 (3.14 to 3.71)	0.04 (0.04 to 0.05)		
Anti-4	4 (3.67 to 4.35)	5.35 (4.66 to 6.15)		
Anti-5	4.52 (4.24 to 4.83)	0.07 (0.06 to 0.08)		
Anti-6B	1.4 (1.24 to 1.58)	2.07 (1.75 to 2.44)		
Anti-7F	4.08 (3.77 to 4.41)	0.03 (0.03 to 0.04)		
Anti-9V	3.39 (3.09 to 3.71)	5.09 (4.34 to 5.96)		
Anti-14	5.54 (5.02 to 6.12)	8.51 (7.27 to 9.95)		
Anti-18C	5.8 (5.17 to 6.52)	5.13 (4.31 to 6.11)		
Anti-19F	7.41 (6.67 to 8.23)	2.77 (2.45 to 3.13)		
Anti-23F	1.96 (1.75 to 2.19)	3.94 (3.26 to 4.77)		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-PD Antibody Concentration

End point title	Anti-PD Antibody Concentration

End point description:

Concentration of anti-PD antibody given as GMC expressed in EL.U/mL.

End point type	Secondary

End point timeframe:

One month after administration of 3rd vaccine dose of the pneumococcal conjugate vaccine

End point values	Synflorix Group	Prevenar Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	344	123		
Units: EL.U/mL.				
geometric mean (confidence interval 95%)	1622.4 (1500.8 to 1754)	88.2 (74.7 to 104)		

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations against pneumococcal cross-reactive serotypes

End point title	Antibody concentrations against pneumococcal cross-reactive serotypes

End point description:

Concentration of cross-reactive pneumococcal serotypes 6A and 19A in ug/mL.

End point type	Secondary

End point timeframe:

One month after the administration of the 3rd vaccine dose of the pneumococcal conjugate vaccine

End point values	Synflorix Group	Prevenar Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	344	123		
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-6A	0.38 (0.33 to 0.44)	0.48 (0.36 to 0.63)		
Anti-19A	0.29 (0.25 to 0.33)	0.12 (0.1 to 0.14)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with Opsonophagocytic activity against pneumococcal cross-reactive serotypes

End point title	Number of subjects with Opsonophagocytic activity against pneumococcal cross-reactive serotypes

End point description:

The results were presented as the dilution of serum (opsonic titer) able to sustain 50% killing of live pneumococci under the assay conditions. In this assay the cut-off value for opsonophagocytic activity against pneumococcal cross-reactive serotypes 6A and 19A was defined as >= 8.

End point type	Secondary

End point timeframe:

One month after the administration of the 3rd vaccine dose of the pneumococcal conjugate vaccine

End point values	Synflorix Group	Prevenar Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	162	60		
Units: Subjects				
Opsono-6A (N=158; 60)	134	54		
Opsono-19A (N= 162; 60)	53	7		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-polyribosyl-ribitol phosphate (anti-PRP) antibody concentrations

End point title	Anti-polyribosyl-ribitol phosphate (anti-PRP) antibody concentrations

End point description:

Concentration of anti-PRP antibody given as GMC in ug/mL.

End point type	Secondary

End point timeframe:

One month after the administration of the 3rd vaccine dose of the pneumococcal conjugate vaccine

End point values	Synflorix Group	Prevenar Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	175	60		
Units: µg/mL				
geometric mean (confidence interval 95%)	20.131 (16.775 to 24.158)	11.844 (8.542 to 16.424)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with Seroprotection status against PRP

End point title	Number of subjects with Seroprotection status against PRP

End point description:

Seroprotection status is defined as anti-PRP antibody concentrations above 0.15 ug/mL and above 1.0 ug/mL

End point type	Secondary

End point timeframe:

One month after the administration of the 3rd vaccine dose of the pneumococcal conjugate vaccine

End point values	Synflorix Group	Prevenar Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	175	60		
Units: Subjects				
Above 0.15	175	60		
Above 1.0	173	58		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting solicited local symptoms

End point title	Number of subjects reporting solicited local symptoms

End point description:

Solicited local symptoms assessed include pain, redness and swelling.

End point type	Secondary

End point timeframe:

Within 4 days after each vaccination

End point values	Synflorix Group	Prevenar Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	371	129		
Units: Subjects				
Pain	210	72		
Redness	252	84		
Swelling	182	69		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with solicited general symptoms

End point title	Number of subjects with solicited general symptoms

End point description:

Solicited general symptoms assessed include drowsiness, fever, irritability and loss of appetite. Fever was defined as axillary temperature >= 37.5 degrees Celsius.

End point type	Secondary

End point timeframe:

Within 4 days after each vaccination

End point values	Synflorix Group	Prevenar Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	371	129		
Units: Subjects				
Drowsiness	212	65		
Fever	113	33		
Irritability	293	99		
Loss of Appetite	177	66		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting unsolicited adverse events

End point title	Number of subjects reporting unsolicited adverse events

End point description:

An unsolicited AE covers 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 and 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. Any was defined as the occurrence of any unsolicited AE regardless of intensity grade or relation to vaccination. Grade 3 AE = an AE which prevented normal, everyday activities. Related = AE assessed by the investigator as related to the vaccination.

End point type	Secondary

End point timeframe:

Within 31 days after each vaccination

End point values	Synflorix Group	Prevenar Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	374	129		
Units: Subjects	213	62		

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

An SAE is any untoward medical occurrence that: results in death, is life-threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, is a congenital anomaly/birth defect in the offspring of a study subject, or may evolve into one of the outcomes listed above.

End point type	Secondary

End point timeframe:

Following the administration of the first dose of the study vaccines throughout the entire study period up to study month 5

End point values	Synflorix Group	Prevenar Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	374	129		
Units: Subjects	56	9		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to study Month 5

Adverse event reporting additional description:

Analysis was performed on the Total Vaccinated Cohort, on subjects with available data. 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

Dictionary used

Dictionary name	MedDRA
Dictionary version	12.0

Reporting groups

Reporting group title	Synflorix Group

Reporting group description:

Subjects received 3 doses of Synflorix vaccine co-administered with Hiberix vaccine at Study Months 0, 2 and 4

Reporting group title	Prevenar Group

Reporting group description:

Subjects received 3 doses of Prevenar vaccine co-administered with Hiberix vaccine at Study Months 0, 2 and 4

Serious adverse events	Synflorix Group	Prevenar Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	56 / 374 (14.97%)	9 / 129 (6.98%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Nervous system disorders			
Febrile convulsion			
subjects affected / exposed	0 / 374 (0.00%)	1 / 129 (0.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	2 / 374 (0.53%)	0 / 129 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Intussusception			

subjects affected / exposed	2 / 374 (0.53%)	1 / 129 (0.78%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enteritis			
subjects affected / exposed	1 / 374 (0.27%)	1 / 129 (0.78%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hepatitis			
subjects affected / exposed	1 / 374 (0.27%)	0 / 129 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Hydronephrosis			
subjects affected / exposed	2 / 374 (0.53%)	0 / 129 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bronchiolitis			
subjects affected / exposed	22 / 374 (5.88%)	1 / 129 (0.78%)	
occurrences causally related to treatment / all	0 / 22	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	8 / 374 (2.14%)	3 / 129 (2.33%)	
occurrences causally related to treatment / all	0 / 8	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	9 / 374 (2.41%)	1 / 129 (0.78%)	
occurrences causally related to treatment / all	0 / 9	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	4 / 374 (1.07%)	1 / 129 (0.78%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Croup infections			
subjects affected / exposed	2 / 374 (0.53%)	1 / 129 (0.78%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis aseptic			
subjects affected / exposed	2 / 374 (0.53%)	1 / 129 (0.78%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngitis			
subjects affected / exposed	3 / 374 (0.80%)	0 / 129 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopneumonia			
subjects affected / exposed	2 / 374 (0.53%)	0 / 129 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis rotavirus			
subjects affected / exposed	2 / 374 (0.53%)	0 / 129 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	2 / 374 (0.53%)	0 / 129 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media acute			
subjects affected / exposed	2 / 374 (0.53%)	0 / 129 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis			
subjects affected / exposed	1 / 374 (0.27%)	0 / 129 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Exanthema subitum			

subjects affected / exposed	1 / 374 (0.27%)	0 / 129 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpangina			
subjects affected / exposed	1 / 374 (0.27%)	0 / 129 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injection site abscess			
subjects affected / exposed	1 / 374 (0.27%)	0 / 129 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngitis			
subjects affected / exposed	1 / 374 (0.27%)	1 / 129 (0.78%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis			
subjects affected / exposed	1 / 374 (0.27%)	0 / 129 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasopharyngitis			
subjects affected / exposed	1 / 374 (0.27%)	0 / 129 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media			
subjects affected / exposed	1 / 374 (0.27%)	0 / 129 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			
subjects affected / exposed	1 / 374 (0.27%)	0 / 129 (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 bronchiolitis			

subjects affected / exposed	0 / 374 (0.00%)	1 / 129 (0.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhinitis			
subjects affected / exposed	0 / 374 (0.00%)	1 / 129 (0.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 374 (0.00%)	1 / 129 (0.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	0 / 374 (0.00%)	1 / 129 (0.78%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Synflorix Group	Prevenar Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	293 / 374 (78.34%)	99 / 129 (76.74%)	
General disorders and administration site conditions			
Pain			
alternative assessment type: Systematic			
subjects affected / exposed	210 / 374 (56.15%)	72 / 129 (55.81%)	
occurrences (all)	210	72	
Redness			
alternative assessment type: Systematic			
subjects affected / exposed	252 / 374 (67.38%)	84 / 129 (65.12%)	
occurrences (all)	252	84	
Swelling			
alternative assessment type: Systematic			

subjects affected / exposed	182 / 374 (48.66%)	69 / 129 (53.49%)	
occurrences (all)	182	69	
Drowsiness			
alternative assessment type: Systematic			
subjects affected / exposed	212 / 374 (56.68%)	65 / 129 (50.39%)	
occurrences (all)	212	65	
Fever			
alternative assessment type: Systematic			
subjects affected / exposed	113 / 374 (30.21%)	33 / 129 (25.58%)	
occurrences (all)	113	33	
Irritability			
alternative assessment type: Systematic			
subjects affected / exposed	293 / 374 (78.34%)	99 / 129 (76.74%)	
occurrences (all)	293	99	
Loss of appetite			
alternative assessment type: Systematic			
subjects affected / exposed	177 / 374 (47.33%)	66 / 129 (51.16%)	
occurrences (all)	177	66	
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	44 / 374 (11.76%)	16 / 129 (12.40%)	
occurrences (all)	44	16	
Nasopharyngitis			
subjects affected / exposed	42 / 374 (11.23%)	16 / 129 (12.40%)	
occurrences (all)	42	16	
Bronchiolitis			
subjects affected / exposed	20 / 374 (5.35%)	4 / 129 (3.10%)	
occurrences (all)	20	4	
Pharyngitis			
subjects affected / exposed	23 / 374 (6.15%)	6 / 129 (4.65%)	
occurrences (all)	23	6	
Bronchitis			
subjects affected / exposed	14 / 374 (3.74%)	7 / 129 (5.43%)	
occurrences (all)	14	7	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 February 2008	The protocol has been amended according to comments received from the Korean FDA. In addition, the Detailed Study Title has been corrected.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported