



Clinical trial results:

A phase II, open-label, multicentre study to evaluate the safety and immunogenicity of GSK Biologicals' DTPa-HBV-IPV/Hib-MenC-TT vaccine as a booster dose in children aged 12 to 18 months, previously primed with the same vaccine in the primary vaccination study DTPa-HBV-IPV=Hib-MenC-TT-002 (112157).

Summary

EudraCT number	2010-019253-18
Trial protocol	PL
Global end of trial date	03 December 2010

Results information

Result version number	v3 (current)
This version publication date	18 May 2018
First version publication date	03 January 2015
Version creation reason	<ul style="list-style-type: none">• Correction of full data setMinor corrections of the full study results.

Trial information

Trial identification

Sponsor protocol code	113978
-----------------------	--------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01171989
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	25 March 2011
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 December 2010
Global end of trial reached?	Yes
Global end of trial date	03 December 2010
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Note: Objectives are conditional to having met all the primary and secondary objectives in study DTPa-HBV-IPV=Hib-MenC-TT-002 (112157).

- To demonstrate that GSK Biologicals' DTPa-HBV-IPV/Hib-MenC-TT vaccine is non-inferior to Menjugate co-administered with Infanrix hexa in terms of seroprotection to MenC one month after the booster dose.

- To demonstrate that GSK Biologicals' DTPa-HBV-IPV/Hib-MenC-TT vaccine is non-inferior to Infanrix hexa co-administered with NeisVac-C in terms of seroprotection to PRP and MenC, one month after the booster dose.

Protection of trial subjects:

Vaccines were administered by qualified and trained personnel. Vaccines were administered only to eligible subjects that had no contraindications to any components of the vaccines.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 August 2010
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	Poland: 391
Worldwide total number of subjects	391
EEA total number of subjects	391

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)	391
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 Period (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	GSK2202083A + Synflorix Group

Arm description:

Healthy male and female subjects between, and including, 12 to 18 months of age at the time of booster vaccination, who were primed with 3 doses of GSK2202083A and Synflorix vaccines in the primary study DTPa-HBV-IPV=HIB-MenC-TT-002 (112157), additionally received a booster dose of GSK2202083A vaccine at Day 0 and of Synflorix vaccine at Month 1. Both vaccines were administered intramuscularly in the anterolateral side of the thigh.

Arm type	Experimental
Investigational medicinal product name	GSK2202083A
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 dose at Day 0 in the anterolateral side of the right thigh

Investigational medicinal product name	Synflorix
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 dose at Month 1 in the anterolateral side of the left thigh

Arm title	Infanrix Hexa/Menjugate Group
------------------	-------------------------------

Arm description:

Healthy male and female subjects between, and including, 12 to 18 months of age at the time of booster vaccination, who were primed with 3 doses of Infanrix hexa vaccine and 2 doses of Menjugate vaccine in the primary study DTPa-HBV-IPV=HIB-MenC-TT-002 (112157), additionally received a booster dose of Infanrix hexa vaccine co-administered with Menjugate vaccine at Day 0. Both vaccines were administered intramuscularly in the anterolateral side of the thigh.

Arm type	Active comparator
Investigational medicinal product name	Infanrix hexa
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:	
1 dose at Day 0 in the anterolateral side of the right thigh.	
Investigational medicinal product name	Menjugate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:
1 dose at Day 0 in the anterolateral side of the left thigh.

Arm title	Infanrix hexa/NeisVac-C + Synflorix Group
------------------	---

Arm description:

Healthy male and female subjects between, and including, 12 to 18 months of age at the time of booster vaccination, who were primed with 3 doses of Infanrix hexa vaccine and Synflorix vaccines in the primary study DTPa-HBV-IPV=HIB-MenC-TT-002 (112157), additionally received a booster dose of Infanrix hexa vaccine co-administered with NeisVac-C vaccine at Day 0 and 1 dose of Synflorix vaccine at Month 1. Both vaccines were administered intramuscularly in the anterolateral side of the thigh.

Arm type	Active comparator
Investigational medicinal product name	Infanrix hexa
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:
1 dose at Day 0 in the anterolateral side of the right thigh.

Investigational medicinal product name	Synflorix
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:
1 dose at Month 1 in the anterolateral side of the left thigh

Investigational medicinal product name	NeisVac-C
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:
1 dose at Day 0 in the anterolateral side of the left thigh.

Number of subjects in period 1	GSK2202083A + Synflorix Group	Infanrix Hexa/Menjugate Group	Infanrix hexa/NeisVac-C + Synflorix Group
Started	137	133	121
Completed	137	133	120
Not completed	0	0	1
Lost to follow-up	-	-	1

Baseline characteristics

Reporting groups

Reporting group title	GSK2202083A + Synflorix Group
-----------------------	-------------------------------

Reporting group description:

Healthy male and female subjects between, and including, 12 to 18 months of age at the time of booster vaccination, who were primed with 3 doses of GSK2202083A and Synflorix vaccines in the primary study DTPa-HBV-IPV=HIB-MenC-TT-002 (112157), additionally received a booster dose of GSK2202083A vaccine at Day 0 and of Synflorix vaccine at Month 1. Both vaccines were administered intramuscularly in the anterolateral side of the thigh.

Reporting group title	Infanrix Hexa/Menjugate Group
-----------------------	-------------------------------

Reporting group description:

Healthy male and female subjects between, and including, 12 to 18 months of age at the time of booster vaccination, who were primed with 3 doses of Infanrix hexa vaccine and 2 doses of Menjugate vaccine in the primary study DTPa-HBV-IPV=HIB-MenC-TT-002 (112157), additionally received a booster dose of Infanrix hexa vaccine co-administered with Menjugate vaccine at Day 0. Both vaccines were administered intramuscularly in the anterolateral side of the thigh.

Reporting group title	Infanrix hexa/NeisVac-C + Synflorix Group
-----------------------	---

Reporting group description:

Healthy male and female subjects between, and including, 12 to 18 months of age at the time of booster vaccination, who were primed with 3 doses of Infanrix hexa vaccine and Synflorix vaccines in the primary study DTPa-HBV-IPV=HIB-MenC-TT-002 (112157), additionally received a booster dose of Infanrix hexa vaccine co-administered with NeisVac-C vaccine at Day 0 and 1 dose of Synflorix vaccine at Month 1. Both vaccines were administered intramuscularly in the anterolateral side of the thigh.

Reporting group values	GSK2202083A + Synflorix Group	Infanrix Hexa/Menjugate Group	Infanrix hexa/NeisVac-C + Synflorix Group
Number of subjects	137	133	121
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous			
Units: months			
arithmetic mean	13.7	13.8	13.7
standard deviation	± 0.71	± 0.73	± 0.76
Gender categorical			
Units: Subjects			
Female	71	82	56
Male	66	51	65
Race/Ethnicity			
Units: Subjects			
White-Caucasian/European heritage	137	133	121

Reporting group values	Total		
Number of subjects	391		
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: months			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	209		
Male	182		
Race/Ethnicity			
Units: Subjects			
White-Caucasian/European heritage	391		

End points

End points reporting groups

Reporting group title	GSK2202083A + Synflorix Group
Reporting group description: Healthy male and female subjects between, and including, 12 to 18 months of age at the time of booster vaccination, who were primed with 3 doses of GSK2202083A and Synflorix vaccines in the primary study DTPa-HBV-IPV=HIB-MenC-TT-002 (112157), additionally received a booster dose of GSK2202083A vaccine at Day 0 and of Synflorix vaccine at Month 1. Both vaccines were administered intramuscularly in the anterolateral side of the thigh.	
Reporting group title	Infanrix Hexa/Menjugate Group
Reporting group description: Healthy male and female subjects between, and including, 12 to 18 months of age at the time of booster vaccination, who were primed with 3 doses of Infanrix hexa vaccine and 2 doses of Menjugate vaccine in the primary study DTPa-HBV-IPV=HIB-MenC-TT-002 (112157), additionally received a booster dose of Infanrix hexa vaccine co-administered with Menjugate vaccine at Day 0. Both vaccines were administered intramuscularly in the anterolateral side of the thigh.	
Reporting group title	Infanrix hexa/NeisVac-C + Synflorix Group
Reporting group description: Healthy male and female subjects between, and including, 12 to 18 months of age at the time of booster vaccination, who were primed with 3 doses of Infanrix hexa vaccine and Synflorix vaccines in the primary study DTPa-HBV-IPV=HIB-MenC-TT-002 (112157), additionally received a booster dose of Infanrix hexa vaccine co-administered with NeisVac-C vaccine at Day 0 and 1 dose of Synflorix vaccine at Month 1. Both vaccines were administered intramuscularly in the anterolateral side of the thigh.	

Primary: Number of seroprotected subjects against Polyribosyl-Ribitol-Phosphate (PRP)

End point title	Number of seroprotected subjects against Polyribosyl-Ribitol-Phosphate (PRP)
End point description: A seroprotected subject was defined as a subject with anti-PRP antibody concentrations greater than or equal to (\geq) 0.15 micrograms per milliliter ($\mu\text{g/mL}$).	
End point type	Primary
End point timeframe: At one Month post (Post) booster dose	

End point values	GSK2202083A + Synflorix Group	Infanrix Hexa/Menjugate Group	Infanrix hexa/NeisVac-C + Synflorix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	132	126	114	
Units: Subjects				
Anti-PRP, Post (N=132, 126, 114)	132	126	114	

Statistical analyses

Statistical analysis title	Difference in percentage anti-PRP ≥ 0.15 $\mu\text{g/mL}$
Comparison groups	Infanrix hexa/NeisVac-C + Synflorix Group v GSK2202083A + Synflorix Group
Number of subjects included in analysis	246
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[1]
Parameter estimate	Difference in percentage
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.27
upper limit	2.84

Notes:

[1] - Criterion for evaluation of Non-inferiority: the upper limit of Standardised asymptotic 95% confidence interval lower or equal to 10%

Primary: Number of seroprotected subjects against Neisseria meningitidis serogroup C using baby rabbit complement (rSBA-MenC)

End point title	Number of seroprotected subjects against Neisseria meningitidis serogroup C using baby rabbit complement (rSBA-MenC)
End point description:	A seroprotected subject was defined as a subject with anti-rSBA-MenC titers greater than or equal to (\geq) 1:8.
End point type	Primary
End point timeframe:	At 1 Month post (Post) booster dose.

End point values	GSK2202083A + Synflorix Group	Infanrix Hexa/Menjugate Group	Infanrix hexa/NeisVac-C + Synflorix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	131	124	114	
Units: Subject				
Anti-rSBA-MenC, Post (N=131, 124, 114)	131	124	114	

Statistical analyses

Statistical analysis title	Difference between groups for rSBA-MenC $\geq 1:8$
Statistical analysis description:	The difference between Infanrix hexa/NeisVac-C and GSK2202083A + Synflorix groups in the percentage of subjects with rSBA-MenC titres equal to or above the cut-off value of 1:8 was assessed.
Comparison groups	Infanrix hexa/NeisVac-C + Synflorix Group v GSK2202083A + Synflorix Group

Number of subjects included in analysis	245
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Difference in percentage
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.27
upper limit	2.86

Statistical analysis title	Difference between groups for rSBA-MenC $\geq 1:8$ (2)
-----------------------------------	--

Statistical analysis description:

The difference between Infanrix hexa/Menjugate and GSK2202083A + Synflorix groups in the percentage of subjects with rSBA-MenC titres equal to or above the cut-off value of 1:8 was assessed.

Comparison groups	GSK2202083A + Synflorix Group v Infanrix Hexa/Menjugate Group
Number of subjects included in analysis	255
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Difference in percentage
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.02
upper limit	2.86

Secondary: Number of seropositive subjects for anti-rSBA-MenC

End point title	Number of seropositive subjects for anti-rSBA-MenC
-----------------	--

End point description:

A seropositive subject for anti-rSBA-MenC was defined as a subject with antibody titers greater than or equal to (\geq) 1:128.

End point type	Secondary
----------------	-----------

End point timeframe:

Before (Pre) and 1 Month post (Post) booster dose

End point values	GSK2202083A + Synflorix Group	Infanrix Hexa/Menjugate Group	Infanrix hexa/NeisVac-C + Synflorix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	131	124	114	
Units: Subjects				
Anti-rSBA-MenC, Pre (N=127, 119, 104)	87	46	3	

Anti-rSBA-MenC, Post (N=131, 124, 114)	130	124	114	
--	-----	-----	-----	--

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-rSBA-MenC antibody titres

End point title	Anti-rSBA-MenC antibody titres
End point description: Antibody titres were expressed as geometric mean titres (GMTs) for the seroprotection cut-off value of $\geq 1:8$.	
End point type	Secondary
End point timeframe: Before (Pre) and 1 Month post (Post) booster dose	

End point values	GSK2202083A + Synflorix Group	Infanrix Hexa/Menjugate Group	Infanrix hexa/NeisVac-C + Synflorix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	131	124	114	
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-rSBA-MenC, Pre (N=127, 119, 104)	148.8 (114.4 to 193.5)	55.6 (40.8 to 75.6)	5.4 (4.5 to 6.6)	
Anti-rSBA-MenC, Post (N=131, 124, 114)	2703.4 (2289.6 to 3192.1)	7701.8 (6511.9 to 9109)	2320.4 (2040.3 to 2638.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with polysaccharide N. meningitidis serogroup C antibody (anti-PSC) antibody concentrations equal to or above the cut-off values

End point title	Number of subjects with polysaccharide N. meningitidis serogroup C antibody (anti-PSC) antibody concentrations equal to or above the cut-off values
End point description: The cut-off values assessed were $\geq 0.3 \mu\text{g/mL}$ and $\geq 2 \mu\text{g/mL}$.	
End point type	Secondary
End point timeframe: Before (Pre) and 1 Month post (Post) booster dose	

End point values	GSK2202083A + Synflorix Group	Infanrix Hexa/Menjugate Group	Infanrix hexa/NeisVac-C + Synflorix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	134	126	114	
Units: Subjects				
Anti-PSC \geq 0.3 mg/mL, Pre (N=134, 126, 114)	133	101	0	
Anti-PSC \geq 0.3 mg/mL, Post (N=134, 125, 114)	134	125	114	
Anti-PSC \geq 2 mg/mL, Pre (N=134, 126, 114)	72	21	0	
Anti-PSC \geq 2 mg/mL, Post (N=134, 125, 114)	129	125	114	

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-PSC antibody concentrations

End point title	Anti-PSC antibody concentrations
End point description: Concentrations were expressed as geometric mean concentrations (GMCs) for the seropositivity cut-off value of \geq 0.3 μ g/mL.	
End point type	Secondary
End point timeframe: Before (Pre) and 1 Month post (Post) booster dose	

End point values	GSK2202083A + Synflorix Group	Infanrix Hexa/Menjugate Group	Infanrix hexa/NeisVac-C + Synflorix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	134	126	114	
Units: μ g/mL				
geometric mean (confidence interval 95%)				
Anti-PSC, Pre (N=134, 126, 114)	1.98 (1.69 to 2.31)	0.76 (0.63 to 0.91)	0.15 (0.15 to 0.15)	
Anti-PSC, Post (N=134, 125, 114)	6.91 (6.21 to 7.69)	21.75 (18.9 to 25.04)	17.7 (15.97 to 19.61)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-PRP antibody concentrations \geq the cut-off

End point title	Number of subjects with anti-PRP antibody concentrations \geq the cut-off
End point description: The cut-off value of the assay was an anti-PRP antibody concentration \geq 1 $\mu\text{g/mL}$.	
End point type	Secondary
End point timeframe: Before (Pre) and 1 Month post (Post) booster dose	

End point values	GSK2202083A + Synflorix Group	Infanrix Hexa/Menjugate Group	Infanrix hexa/NeisVac-C + Synflorix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	134	126	114	
Units: Subjects				
Anti-PRP, Pre (N=134, 125, 113)	32	22	15	
Anti-PRP, Post (N=132, 126, 114)	132	126	114	

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-PRP antibody concentrations

End point title	Anti-PRP antibody concentrations
End point description: Concentrations were expressed as geometric mean concentrations (GMCs) for the cut-off value of \geq 0.15 $\mu\text{g/mL}$.	
End point type	Secondary
End point timeframe: Before (Pre) and 1 Month post (Post) booster dose	

End point values	GSK2202083A + Synflorix Group	Infanrix Hexa/Menjugate Group	Infanrix hexa/NeisVac-C + Synflorix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	134	126	114	
Units: $\mu\text{g/mL}$				
geometric mean (confidence interval 95%)				
Anti-PRP, Pre (N=134, 125, 113)	0.601 (0.502 to 0.719)	0.315 (0.252 to 0.394)	0.368 (0.302 to 0.449)	

Anti-PRP, Post (N=132, 126, 114)	25.449 (21.797 to 29.712)	24.862 (20.188 to 30.619)	25.943 (21.363 to 31.504)	
----------------------------------	---------------------------	---------------------------	---------------------------	--

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seropositive subjects for anti-diphtheria (anti-D) and anti-tetanus (anti-T)

End point title	Number of seropositive subjects for anti-diphtheria (anti-D) and anti-tetanus (anti-T)
End point description: A seropositive subject was defined as a subject with anti-D and anti-T antibody concentrations ≥ 0.1 international units per milliliter (IU/mL).	
End point type	Secondary
End point timeframe: Before (Pre) and 1 Month post (Post) booster dose	

End point values	GSK2202083A + Synflorix Group	Infanrix Hexa/Menjugate Group	Infanrix hexa/NeisVac-C + Synflorix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	134	126	114	
Units: Subjects				
Anti-D, Pre (N=134, 125, 113)	129	115	108	
Anti-D, Post (N=132, 126, 114)	132	126	114	
Anti-T, Pre (N=134, 125, 112)	133	118	111	
Anti-T, Post (N=132, 126, 114)	132	126	114	

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-D and anti-T antibody concentrations

End point title	Anti-D and anti-T antibody concentrations
End point description: Concentrations were expressed as geometric mean concentrations (GMCs) for the seropositivity cut-off value of ≥ 0.1 IU/mL.	
End point type	Secondary
End point timeframe: Before (Pre) and 1 Month post (Post) booster dose	

End point values	GSK2202083A + Synflorix Group	Infanrix Hexa/Menjugate Group	Infanrix hexa/NeisVac-C + Synflorix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	134	126	114	
Units: IU/mL				
geometric mean (confidence interval 95%)				
Anti-D, Pre (N=134, 125, 113)	0.349 (0.308 to 0.395)	0.316 (0.27 to 0.37)	0.311 (0.274 to 0.354)	
Anti-D, Post (N=132, 126, 114)	6.166 (5.47 to 6.951)	7.351 (6.63 to 8.15)	6.02 (5.367 to 6.752)	
Anti-T, Pre (N=134, 125, 112)	0.895 (0.808 to 0.992)	0.316 (0.275 to 0.365)	0.567 (0.5 to 0.643)	
Anti-T, Post (N=132, 126, 114)	11.945 (10.898 to 13.094)	5.351 (4.752 to 6.027)	11.638 (10.398 to 13.025)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-hepatitis B (Anti-HBs) antibody concentrations equal to or above the cut-off values

End point title	Number of subjects with anti-hepatitis B (Anti-HBs) antibody concentrations equal to or above the cut-off values
End point description: The cut-off values assessed were 3.3 milli-international units per milliliter (mIU/mL), 10 mIU/mL and 100 mIU/mL.	
End point type	Secondary
End point timeframe: Before (Pre) and 1 Month post (Post) booster dose	

End point values	GSK2202083A + Synflorix Group	Infanrix Hexa/Menjugate Group	Infanrix hexa/NeisVac-C + Synflorix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	125	122	111	
Units: Subjects				
Anti-HBs \geq 3.3 mIU/mL, Pre (N=124; 122; 105)	123	120	104	
Anti-HBs \geq 10 mIU/mL, Pre (N=124; 122; 105)	121	119	102	
Anti-HBs \geq 100 mIU/mL, Pre (N=124; 122; 105)	99	108	90	

Anti-HBs \geq 3.3 mIU/mL, Post (N=125; 114; 111)	125	114	111	
Anti-HBs \geq 10 mIU/mL, Post (N=125; 114; 111)	125	114	109	
Anti-HBs \geq 100 mIU/mL, Post (N=125; 114; 111)	123	113	109	

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-HBs antibody concentrations

End point title	Anti-HBs antibody concentrations
End point description: Concentrations were presented as geometric mean concentrations (GMCs), expressed in mIU/mL.	
End point type	Secondary
End point timeframe: Before (Pre) and 1 Month post (Post) booster dose	

End point values	GSK2202083A + Synflorix Group	Infanrix Hexa/Menjugate Group	Infanrix hexa/NeisVac-C + Synflorix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	125	122	111	
Units: mIU/mL				
geometric mean (confidence interval 95%)				
Anti-HBs, Pre (N=124; 122; 105)	295.1 (234 to 372.1)	387.6 (302.6 to 496.3)	330.4 (256.5 to 425.5)	
Anti-HBs, Post (N=125; 114; 111)	6390.7 (5171.5 to 7897.2)	8465 (6827 to 10496.1)	6840.3 (5235.8 to 8936.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seropositive subjects for anti-poliovirus types 1, 2 and 3

End point title	Number of seropositive subjects for anti-poliovirus types 1, 2 and 3
End point description: A seropositive subject was defined as a subject with anti-polio type 1, 2 or 3 \geq 1:8.	
End point type	Secondary
End point timeframe: Before (Pre) and 1 Month post (Post) booster dose	

End point values	GSK2202083A + Synflorix Group	Infanrix Hexa/Menjugate Group	Infanrix hexa/NeisVac-C + Synflorix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	113	102	95	
Units: Subjects				
Anti-polio 1, Pre (N=103; 101; 88)	96	96	79	
Anti-polio 1, Post (N=113; 99; 94)	113	99	94	
Anti-polio 2, Pre (N=104; 100; 88)	93	95	80	
Anti-polio 2, Post (N=113; 100; 94)	113	100	94	
Anti-polio 3, Pre (N=102; 102; 88)	94	94	80	
Anti-polio 3, Post (N=113; 100; 95)	113	100	95	

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-poliovirus types 1, 2 and 3 antibody titres

End point title	Anti-poliovirus types 1, 2 and 3 antibody titres
End point description:	
Titers were expressed as geometric mean titters (GMTs) for the seropositivity cut-off value of $\geq 1:8$.	
End point type	Secondary
End point timeframe:	
Before (Pre) and 1 Month post (Post) booster dose	

End point values	GSK2202083A + Synflorix Group	Infanrix Hexa/Menjugate Group	Infanrix hexa/NeisVac-C + Synflorix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	113	102	95	
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-polio 1, Pre (N=103; 101; 88)	35.1 (27.8 to 44.4)	48.3 (37.3 to 62.6)	37 (28.5 to 48)	
Anti-polio 1, Post (N=113; 99; 94)	870.5 (721.5 to 1050.2)	1203 (982.3 to 1473.2)	896.7 (739.1 to 1088)	
Anti-polio 2, Pre (N=104; 100; 88)	34.9 (27.6 to 44.2)	46.2 (35.2 to 60.8)	38.2 (29.2 to 50.1)	
Anti-polio 2, Post (N=113; 100; 94)	1179.1 (979.3 to 1419.7)	1483.6 (1217.2 to 1808.5)	1143.8 (929.7 to 1407.1)	
Anti-polio 3, Pre (N=102; 102; 88)	43.7 (34 to 56.1)	51.6 (39.6 to 67.1)	48.5 (36.3 to 64.7)	

Anti-polio 3, Post (N=113; 100; 95)	1493.3 (1195 to 1866)	1832.9 (1507.9 to 2228.1)	1416.8 (1157.1 to 1734.8)	
-------------------------------------	-----------------------	---------------------------	---------------------------	--

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seropositive subjects for anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin (anti-FHA) and anti-pertactin (anti-PRN)

End point title	Number of seropositive subjects for anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin (anti-FHA) and anti-pertactin (anti-PRN)
End point description:	A seropositive subject was defined as a subject with anti-PT, anti-FHA and anti-PRN antibody concentrations ≥ 5 enzyme-linked immunosorbent assay (ELISA) units per milliliter (EL.U/mL).
End point type	Secondary
End point timeframe:	Before (Pre) and 1 Month post (Post) booster

End point values	GSK2202083A + Synflorix Group	Infanrix Hexa/Menjugate Group	Infanrix hexa/NeisVac-C + Synflorix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	133	126	114	
Units: Subjects				
Anti-PT, Pre (N=133, 125, 112)	98	97	84	
Anti-PT, Post (N=133, 126, 114)	133	126	114	
Anti-FHA, Pre (N=132, 125, 112)	131	122	111	
Anti-FHA, Post (N=132, 126, 114)	132	126	114	
Anti-PRN, Pre (N=133, 126, 113)	100	109	94	
Anti-PRN, Post (N=132, 126, 113)	132	126	113	

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-PT, anti-FHA and anti-PRN antibody concentrations

End point title	Anti-PT, anti-FHA and anti-PRN antibody concentrations
End point description:	Concentrations were expressed as geometric mean concentrations (GMCs) for the seropositivity cut-off value ≥ 5 EL.U/mL.
End point type	Secondary
End point timeframe:	Before (Pre) and 1 Month post (Post) booster

End point values	GSK2202083A + Synflorix Group	Infanrix Hexa/Menjugate Group	Infanrix hexa/NeisVac-C + Synflorix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	133	126	114	
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PT, Pre (N=133, 125, 112)	7.7 (6.7 to 8.8)	8.9 (7.7 to 10.2)	7.1 (6.2 to 8.1)	
Anti-PT, Post (N=133, 126, 114)	50.6 (45.1 to 56.7)	66.3 (58.6 to 75)	61.8 (53.7 to 71.1)	
Anti-FHA, Pre (N=132, 125, 112)	24.3 (21 to 28.2)	30.4 (26.2 to 35.4)	25.7 (22.1 to 29.7)	
Anti-FHA, Post (N=132, 126, 114)	265.3 (235.3 to 299)	339.6 (300.2 to 384.1)	325.2 (284.7 to 371.4)	
Anti-PRN, Pre (N=133, 126, 113)	8.8 (7.5 to 10.3)	12.7 (10.9 to 14.9)	11 (9.3 to 13)	
Anti-PRN, Post (N=132, 126, 113)	216.8 (183.7 to 255.8)	319.8 (275.6 to 371.2)	277.9 (233.1 to 331.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any solicited local symptoms

End point title	Number of subjects with any solicited local symptoms
-----------------	--

End point description:

Solicited local symptoms assessed included pain, redness and swelling. Any= all reports of the specified symptom irrespective of intensity grade.

End point type	Secondary
----------------	-----------

End point timeframe:

During the 8-day (Days 0-7) follow-up period following the booster dose

End point values	GSK2202083A + Synflorix Group	Infanrix Hexa/Menjugate Group	Infanrix hexa/NeisVac-C + Synflorix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	136	133	120	
Units: Subjects				
Any Pain	44	68	58	
Any Redness	69	77	69	
Any Swelling	50	58	50	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any solicited general symptoms

End point title	Number of subjects with any solicited general symptoms
-----------------	--

End point description:

Solicited general symptoms assessed included drowsiness, irritability, loss of appetite and fever (defined as axillary temperature $\geq 37.5^{\circ}\text{C}$). Any= all reports of the specified symptom irrespective of intensity grade and relationship to vaccination.

End point type	Secondary
----------------	-----------

End point timeframe:

During the 8-day (Days 0-7) follow-up period following the booster dose

End point values	GSK2202083A + Synflorix Group	Infanrix Hexa/Menjugate Group	Infanrix hexa/NeisVac-C + Synflorix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	136	133	120	
Units: Subjects				
Any Drowsiness	40	39	39	
Any Irritability	65	65	66	
Any Loss of appetite	31	32	43	
Any Temperature (Axillary)	34	30	31	

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

An unsolicited AE was any AE (i.e. any untoward medical occurrence in a patient or clinical investigation subject, temporally associated with use of a medicinal product, whether or not considered related to the medicinal product) 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
----------------	-----------

End point timeframe:

During the 31-day (Days 0-30) follow-up period following the booster dose

End point values	GSK2202083A + Synflorix Group	Infanrix Hexa/Menjugate Group	Infanrix hexa/NeisVac-C + Synflorix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	137	133	121	
Units: Subjects				
Any AEs	45	29	35	

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of subjects with serious adverse events (SAEs)
End point description: SAEs were defined as medical occurrences that resulted in death, were life threatening, required hospitalization or prolongation of hospitalization or resulted in disability/incapacity.	
End point type	Secondary
End point timeframe: After the booster dose of the study vaccine up to the study end	

End point values	GSK2202083A + Synflorix Group	Infanrix Hexa/Menjugate Group	Infanrix hexa/NeisVac-C + Synflorix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	137	133	121	
Units: Subjects				
Any SAEs	3	2	2	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seropositive subjects for anti-PRP

End point title	Number of seropositive subjects for anti-PRP
End point description: A seropositive subject was defined as a subject with anti-PRP antibody concentrations ≥ 0.15 µg/mL.	
End point type	Secondary
End point timeframe: Before (Pre) booster dose	

End point values	GSK2202083A + Synflorix Group	Infanrix Hexa/Menjugate Group	Infanrix hexa/NeisVac-C + Synflorix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	134	125	113	
Units: Subjects				
Anti-PRP, Pre (N=134, 125, 113)	131	89	88	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroprotected subjects against Neisseria meningitidis serogroup C using baby rabbit complement (rSBA-MenC)

End point title	Number of seroprotected subjects against Neisseria meningitidis serogroup C using baby rabbit complement (rSBA-MenC)
-----------------	--

End point description:

A seroprotected subject was defined as a subject with anti-rSBA-MenC titers greater than or equal to (\geq) 1:8.

End point type	Secondary
----------------	-----------

End point timeframe:

Before (Pre) booster dose

End point values	GSK2202083A + Synflorix Group	Infanrix Hexa/Menjugate Group	Infanrix hexa/NeisVac-C + Synflorix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	127	119	104	
Units: Subjects				
Anti-rSBA-MenC, Pre (N=127, 119, 104)	117	92	10	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited local and general symptoms: during the 8-day (Days 0- 7) post-booster vaccination. Unsolicited adverse events: during the 31-day (Days 0- 30) post-booster vaccination. Serious adverse events: entire booster period (from Month 0 up to Month 1).

Adverse event reporting additional description:

The number of occurrences reported for solicited symptoms, adverse events, and serious adverse events were not available for posting. The number of subjects affected by each specific event was indicated as the number of occurrences.

Assessment type	Systematic
-----------------	------------

Dictionary used

Dictionary name	MedDRA
Dictionary version	13.1

Reporting groups

Reporting group title	Infanrix hexa/NeisVac-C + Synflorix Group
-----------------------	---

Reporting group description:

Healthy male and female subjects between, and including, 12 to 18 months of age at the time of booster vaccination, who were primed with 3 doses of Infanrix hexa vaccine and Synflorix vaccines in the primary study DTPa-HBV-IPV=HIB-MenC-TT-002 (112157), additionally received a booster dose of Infanrix hexa vaccine co-administered with NeisVac-C vaccine at Day 0 and 1 dose of Synflorix vaccine at Month 1. Both vaccines were administered intramuscularly in the anterolateral side of the thigh.

Reporting group title	GSK2202083A + Synflorix Group
-----------------------	-------------------------------

Reporting group description:

Healthy male and female subjects between, and including, 12 to 18 months of age at the time of booster vaccination, who were primed with 3 doses of GSK2202083A and Synflorix vaccines in the primary study DTPa-HBV-IPV=HIB-MenC-TT-002 (112157), additionally received a booster dose of GSK2202083A vaccine at Day 0 and of Synflorix vaccine at Month 1. Both vaccines were administered intramuscularly in the anterolateral side of the thigh.

Reporting group title	Infanrix Hexa/Menjugate Group
-----------------------	-------------------------------

Reporting group description:

Healthy male and female subjects between, and including, 12 to 18 months of age at the time of booster vaccination, who were primed with 3 doses of Infanrix hexa vaccine and 2 doses of Menjugate vaccine in the primary study DTPa-HBV-IPV=HIB-MenC-TT-002 (112157), additionally received a booster dose of Infanrix hexa vaccine co-administered with Menjugate vaccine at Day 0. Both vaccines were administered intramuscularly in the anterolateral side of the thigh.

Serious adverse events	Infanrix hexa/NeisVac-C + Synflorix Group	GSK2202083A + Synflorix Group	Infanrix Hexa/Menjugate Group
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 121 (1.65%)	3 / 137 (2.19%)	2 / 133 (1.50%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Thermal burn			

subjects affected / exposed	0 / 121 (0.00%)	2 / 137 (1.46%)	0 / 133 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 121 (0.83%)	1 / 137 (0.73%)	0 / 133 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	1 / 121 (0.83%)	0 / 137 (0.00%)	1 / 133 (0.75%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 121 (0.83%)	0 / 137 (0.00%)	1 / 133 (0.75%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopneumonia			
subjects affected / exposed	0 / 121 (0.00%)	1 / 137 (0.73%)	0 / 133 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 121 (0.00%)	1 / 137 (0.73%)	0 / 133 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 121 (0.00%)	0 / 137 (0.00%)	1 / 133 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Infanrix hexa/NeisVac-C + Synflorix Group	GSK2202083A + Synflorix Group	Infanrix Hexa/Menjugate Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	102 / 121 (84.30%)	114 / 137 (83.21%)	114 / 133 (85.71%)
General disorders and administration site conditions			
Pain			
subjects affected / exposed ^[1]	58 / 121 (47.93%)	44 / 136 (32.35%)	68 / 133 (51.13%)
occurrences (all)	58	44	68
Redness			
subjects affected / exposed ^[2]	69 / 120 (57.50%)	69 / 136 (50.74%)	77 / 133 (57.89%)
occurrences (all)	69	69	77
Swelling			
subjects affected / exposed ^[3]	50 / 120 (41.67%)	50 / 136 (36.76%)	58 / 133 (43.61%)
occurrences (all)	50	50	58
Drowsiness			
subjects affected / exposed ^[4]	39 / 120 (32.50%)	40 / 136 (29.41%)	39 / 133 (29.32%)
occurrences (all)	39	40	39
Irritability			
subjects affected / exposed ^[5]	66 / 120 (55.00%)	65 / 136 (47.79%)	65 / 133 (48.87%)
occurrences (all)	66	65	65
Loss of appetite			
subjects affected / exposed ^[6]	43 / 120 (35.83%)	31 / 136 (22.79%)	32 / 133 (24.06%)
occurrences (all)	43	31	32
Fever			
subjects affected / exposed ^[7]	31 / 120 (25.83%)	34 / 136 (25.00%)	30 / 133 (22.56%)
occurrences (all)	31	34	30
Infections and infestations			
Upper respiratory tract infection (unsolicited)			
subjects affected / exposed	6 / 121 (4.96%)	6 / 137 (4.38%)	11 / 133 (8.27%)
occurrences (all)	6	6	11
Rhinitis			
subjects affected / exposed	8 / 121 (6.61%)	9 / 137 (6.57%)	4 / 133 (3.01%)
occurrences (all)	8	9	4
Nasopharyngitis			
subjects affected / exposed	4 / 121 (3.31%)	7 / 137 (5.11%)	2 / 133 (1.50%)
occurrences (all)	4	7	2

Pharyngitis			
subjects affected / exposed	6 / 121 (4.96%)	3 / 137 (2.19%)	3 / 133 (2.26%)
occurrences (all)	6	3	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 was performed on the Total vaccinated cohort, only on subjects with their symptom sheets 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: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheets 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: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheets 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: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheets 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: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheets 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: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheets 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: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheets 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