Clinical trial results:
A phase IIIa single-blind, controlled multicentre study to assess the safety, reactogenicity and immunogenicity of GSK Biologicals 10-valent pneumococcal conjugate vaccine or Prevenar when given as a fourth dose between 12-18 months of age in children previously vaccinated in infancy in the primary study 10PN-PD-DIT-001 (105553) with either GSK Biologicals 10-valent pneumococcal conjugate vaccine or Prevenar

Summary

EudraCT number	2006-001628-38
Trial protocol	FI FR
Global end of trial date	06 November 2007

Results information

Result version number	v3 (current)
This version publication date	15 March 2023
First version publication date	29 April 2015
Version creation reason	• Correction of full data set Correction of full data set and alignment between registries.

Trial information

Trial identification

Sponsor protocol code	107046

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00370396
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline Biologicals
Sponsor organisation address	Rue de l'Institut 89, Rixensart, Belgium, B-1330
Public contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089904466, GSKClinicalSupportHD@gsk.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	13 June 2008
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	06 November 2007
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate that a booster dose of GSK Biologicals' 10-valent pneumococcal conjugate vaccine is non-inferior to Prevenar, both co-administered with DTPa-HBV-IPV/Hib vaccine, in terms of post-immunization febrile reactions with rectal fever > 39.0°C.
Criteria for safety:
Non-inferiority will be demonstrated if the upper limit of the 95% CI of the difference (10Pn-10Pn group minus 7Pn-7Pn group), in terms of percentage of subjects with rectal fever >39.0°C, is lower than 10%.

Protection of trial subjects:

All subjects were supervised after vaccination/product administration with appropriate medical treatment readily available. Vaccines/products were administered by qualified and trained personnel. Vaccines/products were administered only to eligible subjects that had no contraindications to any components of the vaccines/products. Towards ensuring the safety of subjects, the study design included an Active Primary Phase (Months 0-1) followed by an additional 5-months Extended Safety Follow-up Phase (ESFU) (up to 6 months after the last vaccination/product administration). Prior to vaccination, subjects' pre-vaccination body temperature was also evaluated.

Background therapy: -	
Evidence for comparator: -	
Actual start date of recruitment	25 September 2006
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	5 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Finland: 398
Country: Number of subjects enrolled	France: 142
Country: Number of subjects enrolled	Poland: 572
Worldwide total number of subjects	1112
EEA total number of subjects	1112

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)	1112
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:

This study consisted of approximately 1200 subjects who were previously enrolled and had been vaccinated with either the 10Pn or 7Pn vaccine as part of the 10PN-PD-DIT-001 (105553) study (EudraCTnumber: 2005-003300-11).

Pre-assignment

Screening details:

During the screening the following was performed: informed consent was obtained and signed from parents or guardians of subjects, check for inclusion/exclusion criteria and contraindications/precautions was performed, and medical history of subjects was collected. Prior to vaccination, subjects' pre-vaccination body temperature was evaluated.

Period 1

Period 1 title	Overall Study Period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Synflorix-Synflorix Group

Arm description:

This group consisted of subjects previously vaccinated with the Synflorix vaccine as part of a previous study by GSK Biologicals – the 10PN-PD-DIT-001 (105553) study (EuDRA-CT number: 2005-003300-11). As part of the 105553 study, subjects had received a 3-dose primary vaccination of Synflorix vaccine at 2, 3 and 4 months of age (injected intramuscularly [IM] in the right thigh) co-administered with Infanrix hexa vaccine, except for the second dose in France, which was co-administered with Infanrix IPV Hib, injected intramuscularly in the left thigh. As part of this study, at 12-18 months of age, subjects received a booster dose of Synflorix vaccine, injected IM in the right thigh or deltoid, co-administered with Infanrix hexa vaccine, injected IM in the left thigh or deltoid.

Arm type	Experimental
Investigational medicinal product name	10 valent streptococcus pneumoniae conjugate vaccine
Investigational medicinal product code	
Other name	10Pn-PD-DiT, Synflorix (by GSK Biologicals)
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

One dose administered at 12-18 months of age in the left thigh or deltoid.

Investigational medicinal product name	DTPa-HBV-IPV/Hib
Investigational medicinal product code	
Other name	Infanrix hexa (by GSK Biologicals)
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

One dose administered at at 12-18 months of age in the right thigh or deltoid.

Arm title	Prevenar-Prevenar Group

Arm description:

This group consisted of subjects previously vaccinated with the Prevenar vaccine as part of a previous study by GSK Biologicals – the 10PN-PD-DIT-001 (105553) study (EuDRA-CT number: 2005-003300-11). As part of the 105553 study, subjects had received a 3-dose primary vaccination of Prevenar vaccine at 2, 3 and 4 months of age (injected intramuscularly [IM] in the right thigh) co-administered with Infanrix hexa vaccine, except for the second dose in France, which was co-administered with

Infanrix IPV Hib, injected intramuscularly in the left thigh. As part of this study, at 12-18 months of age, subjects received a booster dose of Prevenar vaccine, injected IM in the right thigh or deltoid, co-administered with Infanrix hexa vaccine, injected IM in the left thigh or deltoid.

Arm type	Active comparator
Investigational medicinal product name	7Pn
Investigational medicinal product code	
Other name	Prevenar by Wyeth Lederle Vaccines S.A.
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

One dose administered at 12-18 months of age in the left thigh or deltoid.

Investigational medicinal product name	DTPa-HBV-IPV/Hib
Investigational medicinal product code	
Other name	Infanrix hexa (by GSK Biologicals)
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

One dose administered at at 12-18 months of age in the right thigh or deltoid.

Arm title	Prevenar-Synflorix Group

Arm description:

This group consisted of subjects previously vaccinated with the Prevenar vaccine as part of a previous study by GSK Biologicals – the 10PN-PD-DIT-001 (105553) study (EuDRA-CT number: 2005-003300-11). As part of the 105553 study, subjects had received a 3-dose primary vaccination of Synflorix vaccine at 2, 3 and 4 months of age (injected intramuscularly [IM] in the right thigh) co-administered with Infanrix hexa vaccine, except for the second dose in France, which was co-administered with Infanrix IPV Hib, injected intramuscularly in the left thigh. As part of this study, at 12-18 months of age, subjects received a booster dose of Synflorix, injected IM in the right thigh or deltoid, co-administered with Infanrix hexa vaccine, injected IM in the left thigh or deltoid.

Arm type	Active comparator
Investigational medicinal product name	10 valent streptococcus pneumoniae conjugate vaccine
Investigational medicinal product code	
Other name	10Pn-PD-DiT, Synflorix (by GSK Biologicals)
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

One dose administered at 12-18 months of age in the left thigh or deltoid.

Investigational medicinal product name	DTPa-HBV-IPV/Hib
Investigational medicinal product code	
Other name	Infanrix hexa (by GSK Biologicals)
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

One dose administered at at 12-18 months of age in the right thigh or deltoid.

Number of subjects in period 1	Synflorix-Synflorix Group	Prevenar-Prevenar Group	Prevenar-Synflorix Group
Started	737	92	283
Overall Study Period	737	92	283
Completed	726	91	282
Not completed	11	1	1

Consent withdrawn by subject	-	-	1
Lost to follow-up	11	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Synflorix-Synflorix Group
Reporting group description:	
This group consisted of subjects previously vaccinated with the Synflorix vaccine as part of a previous study by GSK Biologicals – the 10PN-PD-DIT-001 (105553) study (EuDRA-CT number: 2005-003300-11). As part of the 105553 study, subjects had received a 3-dose primary vaccination of Synflorix vaccine at 2, 3 and 4 months of age (injected intramuscularly [IM] in the right thigh) co-administered with Infanrix hexa vaccine, except for the second dose in France, which was co-administered with Infanrix IPV Hib, injected intramuscularly in the left thigh. As part of this study, at 12-18 months of age, subjects received a booster dose of Synflorix vaccine, injected IM in the right thigh or deltoid, co-administered with Infanrix hexa vaccine, injected IM in the left thigh or deltoid.	
Reporting group title	Prevenar-Prevenar Group
Reporting group description:	
This group consisted of subjects previously vaccinated with the Prevenar vaccine as part of a previous study by GSK Biologicals – the 10PN-PD-DIT-001 (105553) study (EuDRA-CT number: 2005-003300-11). As part of the 105553 study, subjects had received a 3-dose primary vaccination of Prevenar vaccine at 2, 3 and 4 months of age (injected intramuscularly [IM] in the right thigh) co-administered with Infanrix hexa vaccine, except for the second dose in France, which was co-administered with Infanrix IPV Hib, injected intramuscularly in the left thigh. As part of this study, at 12-18 months of age, subjects received a booster dose of Prevenar vaccine, injected IM in the right thigh or deltoid, co-administered with Infanrix hexa vaccine, injected IM in the left thigh or deltoid.	
Reporting group title	Prevenar-Synflorix Group
Reporting group description:	
This group consisted of subjects previously vaccinated with the Prevenar vaccine as part of a previous study by GSK Biologicals – the 10PN-PD-DIT-001 (105553) study (EuDRA-CT number: 2005-003300-11). As part of the 105553 study, subjects had received a 3-dose primary vaccination of Synflorix vaccine at 2, 3 and 4 months of age (injected intramuscularly [IM] in the right thigh) co-administered with Infanrix hexa vaccine, except for the second dose in France, which was co-administered with Infanrix IPV Hib, injected intramuscularly in the left thigh. As part of this study, at 12-18 months of age, subjects received a booster dose of Synflorix, injected IM in the right thigh or deltoid, co-administered with Infanrix hexa vaccine, injected IM in the left thigh or deltoid.	

Reporting group values	Synflorix-Synflorix Group	Prevenar-Prevenar Group	Prevenar-Synflorix Group
Number of subjects	737	92	283
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	737	92	283
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: months			
geometric mean	15.3	14.2	14.2
standard deviation	± 2.08	± 2.26	± 2.23

Gender categorical Units: Subjects			
Female	360	50	134
Male	377	42	149

Reporting group values	Total		
Number of subjects	1112		
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)	1112		
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			
geometric mean			
standard deviation	-		
Gender categorical Units: Subjects			
Female	544		
Male	568		

End points

End points reporting groups

Reporting group title	Synflorix-Synflorix Group

Reporting group description:

This group consisted of subjects previously vaccinated with the Synflorix vaccine as part of a previous study by GSK Biologicals – the 10PN-PD-DIT-001 (105553) study (EuDRA-CT number: 2005-003300-11). As part of the 105553 study, subjects had received a 3-dose primary vaccination of Synflorix vaccine at 2, 3 and 4 months of age (injected intramuscularly [IM] in the right thigh) co-administered with Infanrix hexa vaccine, except for the second dose in France, which was co-administered with Infanrix IPV Hib, injected intramuscularly in the left thigh. As part of this study, at 12-18 months of age, subjects received a booster dose of Synflorix vaccine, injected IM in the right thigh or deltoid, co-administered with Infanrix hexa vaccine, injected IM in the left thigh or deltoid.

Reporting group title	Prevenar-Prevenar Group

Reporting group description:

This group consisted of subjects previously vaccinated with the Prevenar vaccine as part of a previous study by GSK Biologicals – the 10PN-PD-DIT-001 (105553) study (EuDRA-CT number: 2005-003300-11). As part of the 105553 study, subjects had received a 3-dose primary vaccination of Prevenar vaccine at 2, 3 and 4 months of age (injected intramuscularly [IM] in the right thigh) co-administered with Infanrix hexa vaccine, except for the second dose in France, which was co-administered with Infanrix IPV Hib, injected intramuscularly in the left thigh. As part of this study, at 12-18 months of age, subjects received a booster dose of Prevenar vaccine, injected IM in the right thigh or deltoid, co-administered with Infanrix hexa vaccine, injected IM in the left thigh or deltoid.

Reporting group title	Prevenar-Synflorix Group

Reporting group description:

This group consisted of subjects previously vaccinated with the Prevenar vaccine as part of a previous study by GSK Biologicals – the 10PN-PD-DIT-001 (105553) study (EuDRA-CT number: 2005-003300-11). As part of the 105553 study, subjects had received a 3-dose primary vaccination of Synflorix vaccine at 2, 3 and 4 months of age (injected intramuscularly [IM] in the right thigh) co-administered with Infanrix hexa vaccine, except for the second dose in France, which was co-administered with Infanrix IPV Hib, injected intramuscularly in the left thigh. As part of this study, at 12-18 months of age, subjects received a booster dose of Synflorix, injected IM in the right thigh or deltoid, co-administered with Infanrix hexa vaccine, injected IM in the left thigh or deltoid.

Primary: Number of subjects with rectal temperature above (>) 39.0 degrees Celsius (°C) post booster between the Synflorix-Synflorix and Prevenar-Prevenar groups

End point title	Number of subjects with rectal temperature above (>) 39.0 degrees Celsius (°C) post booster between the Synflorix-Synflorix and Prevenar-Prevenar groups[1]

End point description:

Fever was measured as rectal temperature. Assessment of occurrences of rectal temperature > 39.0 °C was performed post administration of the booster dose of pneumococcal vaccine (Synflorix or Prevenar vaccine) in this study. The analysis was performed on the Total vaccinated cohort, which included all subjects vaccinated in this study 10PN-PD-DIT-007, solely on subjects with results available.

End point type	Primary

End point timeframe:

Within 4 days (Days 0-3) after the booster vaccination at Month 0 in this study 10PN-PD-DIT-007

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is only reporting values for the Synflorix-Synflorix and Prevenar-Prevenar groups.

End point values	Synflorix-Synflorix Group	Prevenar-Prevenar Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	735	91		
Units: Subjects				
Subjects with rectal temperature >39°C	24	7		

Statistical analyses

Statistical analysis title	Non-inferiority of Synflorix vs Prevenar vaccine

Statistical analysis description:

Analysis aimed at demonstrating the non-inferiority of Synflorix vs Prevenar vaccine, both co-administered with Infanrix hexa vaccine, in terms of post-immunization febrile reactions with rectal fever > 39.0°C. Standardized asymptotic 95% confidence interval (CI) for the difference [Synflorix-Synflorix minus Prevenar-Prevenar] in terms of percentages of subjects reporting rectal fever >39.0°C was computed.

Comparison groups	Prevenar-Prevenar Group v Synflorix-Synflorix Group
Number of subjects included in analysis	826
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
Parameter estimate	Difference in percentage
Point estimate	-4.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.85
upper limit	-0.21

Notes:

[2] - Non-inferiority was demonstrated if the upper limit of the computed standardized asymptotic 95% CI was lower than the pre-defined limit of 10%.

Secondary: Number of subjects with any and Grade 3 solicited local symptoms

End point title	Number of subjects with any and Grade 3 solicited local symptoms

End point description:

Solicited local symptoms assessed include pain, redness and swelling. Grade 3 pain was defined as crying when limb was moved/spontaneously painful. Grade 3 swelling/redness was defined as swelling/redness larger than (>) 30 millimeters (mm). "Any" is defined as incidence of the specified symptom regardless of intensity. The analysis was performed on the Total vaccinated cohort, which included all subjects vaccinated in this study 10PN-PD-DIT-007, solely on subjects with results available.

End point type	Secondary

End point timeframe:

Within 4 days (Days 0-3) after the booster vaccination at Month 0 in this study 10PN-PD-DIT-007

End point values	Synflorix-Synflorix Group	Prevenar-Prevenar Group	Prevenar-Synflorix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	735	91	282	
Units: Subjects				
Any Pain	452	48	150	
Grade 3 Pain	47	3	18	
Any Swelling	338	42	112	
Grade 3 Swelling	67	7	20	
Any Redness	451	59	153	
Grade 3 Redness	96	7	19	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any and any Grade 3 solicited general symptoms

End point title	Number of subjects with any and any Grade 3 solicited general symptoms

End point description:

Solicited general symptoms assessed include drowsiness, fever (defined as rectal temperature ≥ 38.0°C), irritability, and loss of appetite. Grade 3 drowsiness was defined as drowsiness which prevented normal everyday activities. Grade 3 fever was defined as fever (rectal temperature) above (>) 40.0 degree Celsius (°C). Grade 3 irritability was defined as crying that could not be comforted/preventing normal everyday activities. Grade 3 loss of appetite was defined as the subject not eating at all. "Any" is defined as incidence of the specified symptom regardless of intensity or relationship to study vaccination. The analysis was performed on the Total vaccinated cohort, which included all subjects vaccinated in this study 10PN-PD-DIT-007, solely on subjects with results available.

End point type	Secondary

End point timeframe:

Within 4 days (Days 0-3) after the booster vaccination at Month 0 in this study 10PN-PD-DIT-007

End point values	Synflorix-Synflorix Group	Prevenar-Prevenar Group	Prevenar-Synflorix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	735	91	282	
Units: Subjects				
Any drowsiness	303	48	130	
Grade 3 drowsiness	5	0	5	
Any fever	245	33	112	
Grade 3 fever	1	2	3	
Any irritability	438	55	176	
Grade 3 irritability	15	2	12	
Any loss of appetite	230	31	92	
Grade 3 loss of appetite	4	0	3	

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 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. "Any" is defined an incidence of an unsolicited AE regardless of intensity or relationship to study vaccination. The analysis was performed on the Total vaccinated cohort, which included all subjects vaccinated in this study 10PN-PD-DIT-007.

End point type	Secondary

End point timeframe:

Within 31 days (Day 0-30) after the booster vaccination at Month 0 in this study 10PN-PD-DIT-007

End point values	Synflorix-Synflorix Group	Prevenar-Prevenar Group	Prevenar-Synflorix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	737	92	283	
Units: Subjects				
Subject(s) with unsolicited AE(s)	188	32	99	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with serious adverse events (SAEs) during the Active Phase of the study

End point title	Number of subjects with serious adverse events (SAEs) during the Active Phase of the study

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, or may evolve into one of the outcomes listed above. "Any" is defined an incidence of a SAE regardless of intensity/severity. The analysis was performed on the Total vaccinated cohort, which included all subjects vaccinated in this study 10PN-PD-DIT-007.

End point type	Secondary

End point timeframe:

Throughout the Active Phase of the study, that is, within 31 days (Day 0-30) after the booster vaccination at Month 0 in this study 10PN-PD-DIT-007

End point values	Synflorix-Synflorix Group	Prevenar-Prevenar Group	Prevenar-Synflorix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	737	92	283	
Units: Subjects				
Subject(s) with SAEs	12	1	4	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with serious adverse events (SAEs) during the entire study

End point title	Number of subjects with serious adverse events (SAEs) during the entire study

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, or may evolve into one of the outcomes listed above. “Any” is defined an incidence of a SAE regardless of intensity/severity. The analysis was performed on the Total vaccinated cohort, which included all subjects vaccinated in this study 10PN-PD-DIT-007, solely on subjects enrolled in the ESFU Phase of the study.

End point type	Secondary

End point timeframe:

Throughout the study period, from Month 0 prior to booster vaccination up to Month 6, end of the ESFU in this study 10PN-PD-DIT-007

End point values	Synflorix-Synflorix Group	Prevenar-Prevenar Group	Prevenar-Synflorix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	726	92	282	
Units: Subjects				
Subject(s) with SAEs	33	6	8	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seroprotected as regards anti-pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F antigens – by 22F-inhibition Enzyme-linked immunosorbent assay (ELISA)

End point title	Number of subjects seroprotected as regards anti-

	pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F antigens – by 22F-inhibition Enzyme-linked immunosorbent assay (ELISA)

End point description:

A seroprotected subject as regards anti-pneumococcal serotype antibody was defined as a subject with anti-pneumococcal serotype antibody concentration greater than or equal to (≥) 0.20 microgram per millilitre (µg/mL). Anti-pneumococcal serotypes antibodies assessed were antibodies against 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). Analysis was performed using the 22F-inhibition Enzyme-linked immunosorbent assay (ELISA), using ≥ 0.05 µg/mL as seropositivity cut off. For this endpoint, the analysis was performed on the according-to-protocol cohort for immunogenicity, e. a., evaluable subjects for whom assay results were available for antibodies against at least one study vaccine antigen component after booster vaccination.

End point type	Secondary

End point timeframe:

Prior to (PRE) and one month after (Month 1) booster vaccination

End point values	Synflorix-Synflorix Group	Prevenar-Prevenar Group	Prevenar-Synflorix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	347	89	134	
Units: Subjects				
Anti-1 PRE (N=338;82;133)	123	3	3	
Anti-1 Month 1 (N=342;81;133)	340	4	113	
Anti-4 PRE (N=342;78;131)	196	53	99	
Anti-4 Month 1 (N=343;88;133)	342	88	133	
Anti-5 PRE (N=344;84;134)	231	5	14	
Anti-5 Month 1 (N=342;82;133)	340	5	114	
Anti-6B PRE (N=333;75;131)	223	23	69	
Anti-6B Month 1 (N=341 ;87;133)	329	85	131	
Anti-7F PRE (N=340;85;133)	308	4	3	
Anti-7F Month 1 (N=342;85;133)	342	6	127	
Anti-9V PRE (N=344;77;130)	291	70	123	
Anti-9V Month 1 (N=340;89;133)	340	89	133	
Anti-14 PRE (N=336;75;130)	268	70	125	
Anti-14 Month 1 (N=339;86;133)	336	86	133	
Anti-18C PRE (N=341;83;131)	240	60	107	
Anti-18C Month 1 (N=343;87;134)	343	87	133	
Anti-19F PRE (N=347;85;134)	272	38	76	
Anti-19F Month 1 (N=343;87;134)	341	87	131	
Anti-23F PRE (N=338;77;130)	206	43	98	
Anti-23F Month 1 (N=341;88;132)	332	87	128	

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations against 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) – by

22F-inhibition Enzyme-linked immunosorbent assay (ELISA)

End point title	Antibody concentrations against 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) – by 22F-inhibition Enzyme-linked immunosorbent assay (ELISA)

End point description:

Anti-pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F antibody concentrations (Anti-1, -4, -5, -6B, -7F, -9V, -14, -18C, -19F and -23F) were calculated, expressed as geometric mean concentrations (GMCs), in microgram per millilitre (µg/mL). The seropositivity cut-off for the assay was ≥ 0.05 µg/mL. Antibody concentrations below the cut-off of the assay were given an arbitrary value of half the cut-off for the purpose of GMC calculation. For this endpoint, the analysis was performed on the according-to-protocol cohort for immunogenicity, e. a., evaluable subjects for whom assay results were available for antibodies against at least one study vaccine antigen component after booster vaccination.

End point type	Secondary

End point timeframe:

Prior to (PRE) and one month (Month 1) post booster vaccination

End point values	Synflorix-Synflorix Group	Prevenar-Prevenar Group	Prevenar-Synflorix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	347	89	134	
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-1 PRE (N=338;82;133)	0.14 (0.13 to 0.16)	0.03 (0.03 to 0.04)	0.03 (0.03 to 0.04)	
Anti-1 Month 1 (N=342;81;133)	1.53 (1.4 to 1.68)	0.04 (0.03 to 0.05)	0.67 (0.56 to 0.8)	
Anti-4 PRE (N=342;78;131)	0.23 (0.21 to 0.26)	0.3 (0.25 to 0.37)	0.35 (0.3 to 0.41)	
Anti-4 Month 1 (N=343;88;133)	3.35 (3.06 to 3.67)	4.4 (3.75 to 5.15)	4.47 (3.85 to 5.19)	
Anti-5 PRE (N=344;84;134)	0.27 (0.25 to 0.3)	0.04 (0.04 to 0.05)	0.05 (0.04 to 0.05)	
Anti-5 Month 1 (N=342;82;133)	2.2 (2 to 2.42)	0.05 (0.04 to 0.07)	0.74 (0.6 to 0.9)	
Anti-6B PRE (N=333;75;131)	0.31 (0.27 to 0.35)	0.14 (0.11 to 0.19)	0.26 (0.2 to 0.33)	
Anti-6B Month 1 (N=341 ;87;133)	1.94 (1.74 to 2.17)	3.53 (2.83 to 4.41)	1.74 (1.48 to 2.05)	
Anti-7F PRE (N=340;85;133)	0.57 (0.52 to 0.62)	0.03 (0.03 to 0.04)	0.03 (0.03 to 0.03)	
Anti-7F Month 1 (N=342;85;133)	3.5 (3.25 to 3.76)	0.04 (0.03 to 0.05)	1.83 (1.49 to 2.24)	
Anti-9V PRE (N=344;77;130)	0.54 (0.48 to 0.6)	0.62 (0.51 to 0.76)	0.78 (0.68 to 0.89)	
Anti-9V Month 1 (N=340;89;133)	3.25 (2.99 to 3.53)	6.09 (5.19 to 7.15)	1.94 (1.73 to 2.19)	
Anti-14 PRE (N=336;75;130)	0.66 (0.56 to 0.76)	1.06 (0.82 to 1.38)	1.69 (1.4 to 2.03)	
Anti-14 Month 1 (N=339;86;133)	5.56 (5.01 to 6.18)	9.29 (7.85 to 10.99)	4.76 (4.12 to 5.49)	
Anti-18C PRE (N=341;83;131)	0.3 (0.28 to 0.34)	0.32 (0.26 to 0.39)	0.37 (0.32 to 0.43)	
Anti-18C Month 1 (N=343;87;134)	5.01 (4.6 to 5.46)	5.21 (4.44 to 6.11)	4.98 (4.17 to 5.93)	

Anti-19F PRE (N=347;85 ;134)	0.53 (0.46 to 0.61)	0.23 (0.17 to 0.31)	0.31 (0.24 to 0.41)	
Anti-19F Month 1 (N=343;87;134)	6.05 (5.46 to 6.71)	3.35 (2.83 to 3.97)	5.06 (4.24 to 6.04)	
Anti-23F PRE (N=338;77;130)	0.27 (0.23 to 0.31)	0.24 (0.19 to 0.31)	0.4 (0.32 to 0.5)	
Anti-23F Month 1 (N=341;88;132)	2.38 (2.13 to 2.66)	6.67 (5.38 to 8.26)	2.42 (1.99 to 2.95)	

Statistical analyses

No statistical analyses for this end point

Secondary: Opsonophagocytic activity (OPA) titers against pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F

End point title	Opsonophagocytic activity (OPA) titers against pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F

End point description:

OPA titers against pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F (Opsono-1, -4, -5, -6B, -7F, -9V, -14, -18C, -19F and -23F) were calculated, expressed as geometric mean titers (GMTs) and tabulated. The seropositivity cut-off for the assay was ≥ 8. Antibody titers below the cut-off of the assay were given an arbitrary value of half the cut-off for the purpose of GMT calculation. For this endpoint, the analysis was performed on the according-to-protocol cohort for immunogenicity, e. a., evaluable subjects for whom assay results were available for antibodies against at least one study vaccine antigen component after booster vaccination.

End point type	Secondary

End point timeframe:

Prior to (PRE) and one month (Month 1) post booster vaccination

End point values	Synflorix-Synflorix Group	Prevenar-Prevenar Group	Prevenar-Synflorix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	326	83	126	
Units: Titer				
geometric mean (confidence interval 95%)				
Opsono-1 PRE (N=326;83;126)	6.1 (5.4 to 6.9)	5 (4.1 to 6)	4.9 (4.2 to 5.8)	
Opsono-1 Month 1 (N=301;83;121)	192.2 (157.5 to 234.6)	4.3 (3.9 to 4.7)	8.3 (6.7 to 10.4)	
Opsono-4 PRE (N=295;79;112)	20.3 (16.2 to 25.5)	24.5 (15.4 to 38.8)	37.8 (24.8 to 57.7)	
Opsono-4 Month 1 (N=297;81;123)	1856.3 (1666.1 to 2068)	2812.6 (2282.5 to 3465.9)	1528.9 (1286.5 to 1817)	
Opsono-5 PRE (N=305;79;124)	8.2 (7.2 to 9.4)	4.4 (3.9 to 4.9)	4.1 (3.9 to 4.3)	
Opsono-5 Month 1 (N=299;83;122)	144.1 (122.1 to 170)	4.1 (3.9 to 4.4)	9.5 (7.5 to 11.9)	
Opsono-6B PRE (N=284;75;120)	60.3 (44.6 to 81.7)	51.4 (27.1 to 97.5)	36.7 (23.3 to 57.7)	
Opsono-6B Month 1 (N=295;79;118)	981.2 (830.7 to 1159.1)	3459.6 (2535.7 to 4720.3)	640.2 (480.7 to 852.7)	

Opsono-7F PRE (N=294;76;117)	377.7 (279.8 to 509.9)	34.8 (17.5 to 69.3)	25.3 (15.4 to 41.6)	
Opsono-7F Month 1 (N=296;74;118)	4330.3 (3836 to 4888.3)	25.2 (13.1 to 48.7)	2397.2 (1929.2 to 2978.7)	
Opsono-9V PRE (N=309;81;122)	296.9 (259.3 to 339.9)	305.5 (227.1 to 411)	305.1 (248.7 to 374.4)	
Opsono-9V Month 1 (N=297;79;120)	2343.5 (2097.1 to 2618.7)	5357.4 (4212.5 to 6813.6)	886.8 (747.7 to 1051.8)	
Opsono-14 PRE (N=299;79;118)	188.1 (149.9 to 235.9)	201.6 (129.4 to 314.2)	391.1 (303.1 to 504.6)	
Opsono-14 Month 1 (N=304;82;123)	2085.9 (1868 to 2329.1)	2134.2 (1689.1 to 2696.6)	977.8 (828.9 to 1153.5)	
Opsono-18C PRE (N=309;82;121)	8.7 (7.4 to 10.3)	10.4 (7.4 to 14.7)	8.5 (6.6 to 10.9)	
Opsono-18C Month 1 (N=299;76;121)	810.3 (712.4 to 921.7)	968.7 (724.1 to 1295.8)	610.7 (480.3 to 776.4)	
Opsono-19F PRE (N=317;81;123)	10.5 (8.9 to 12.3)	5.9 (4.5 to 7.8)	7.3 (5.5 to 9.6)	
Opsono-19F Month 1 (N=293;80;120)	624.3 (509.7 to 764.7)	287.8 (190.8 to 434.3)	530.1 (393 to 715.2)	
Opsono-23F PRE (N=305;77;120)	171.5 (126.3 to 232.8)	205.8 (110.1 to 384.6)	532.9 (344.4 to 824.7)	
Opsono-23F Month 1 (N=301;80;122)	2830.1 (2487.2 to 3220.3)	13900.7 (10177.4 to 18986.1)	2828.8 (2234.3 to 3581.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations to protein D (Anti-PD) - by Enzyme-Linked Immunosorbent Assay (ELISA)

End point title	Antibody concentrations to protein D (Anti-PD) - by Enzyme-Linked Immunosorbent Assay (ELISA)

End point description:

Anti-protein D (Anti-PD) antibody concentrations by Enzyme-Linked Immunosorbent Assay (ELISA) were calculated, expressed as geometric mean concentrations (GMCs) in ELISA unit per milli-liter (EL.U/mL) and tabulated. The seropositivity cut-off for the assay was ≥ 100 EL.U/mL. Antibody concentrations below the cut-off of the assay were given an arbitrary value of half the cut-off for the purpose of GMC calculation. For this endpoint, the analysis was performed on the according-to-protocol cohort for immunogenicity, e. a., evaluable subjects for whom assay results were available for antibodies against at least one study vaccine antigen component after booster vaccination.

End point type	Secondary

End point timeframe:

Prior to (PRE) and one month (Month 1) post booster vaccination

End point values	Synflorix-Synflorix Group	Prevenar-Prevenar Group	Prevenar-Synflorix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	340	86	134	
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PD, PRE (N=338;73;127)	556.4 (494.7 to 625.7)	72.3 (59.3 to 88)	78.1 (67.8 to 89.9)	
Anti-PD, Month 1 (N=340;86;134)	2887.6 (2573.7 to 3239.8)	75.3 (60 to 94.4)	125.5 (103.4 to 152.4)	

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:

Anti-PRP antibody concentrations were calculated, expressed as geometric mean concentrations (GMCs), in microgram per milliliter (µg/mL), and tabulated. The seroprotection cut-off for the assay for the purpose of this endpoint was ≥ 0.15 µg/mL. Antibody concentrations below the cut-off of the assay were given an arbitrary value of half the cut-off for the purpose of GMC calculation. For this endpoint, the analysis was performed on the according-to-protocol cohort for immunogenicity, e. a., evaluable subjects for whom assay results were available for antibodies against at least one study vaccine antigen component after booster vaccination.

End point type	Secondary

End point timeframe:

Prior to (PRE) and one month (Month 1) post booster vaccination

End point values	Synflorix-Synflorix Group	Prevenar-Prevenar Group	Prevenar-Synflorix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	344	46	136	
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-PRP, PRE (N=344;39;136)	0.308 (0.272 to 0.348)	0.231 (0.151 to 0.353)	0.246 (0.2 to 0.304)	
Anti-PRP, Month 1 (N=343;46;136)	36.634 (31.897 to 42.074)	25.731 (15.87 to 41.719)	29.851 (23.563 to 37.816)	

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-pertussis toxoid (Anti-PT), anti- filamentous haemagglutinin (Anti-FHA) and anti-pertactin (Anti-PRN) antibody concentrations

End point title	Anti-pertussis toxoid (Anti-PT), anti- filamentous haemagglutinin (Anti-FHA) and anti-pertactin (Anti-PRN) antibody concentrations

End point description:

Anti-PT, Anti-FHA and Anti-PRN concentrations measured by Enzyme-Linked Immunosorbent Assay (ELISA) were calculated, expressed as geometric mean concentrations (GMCs) in ELISA unit per milli-liter (EL.U/mL) and tabulated. The seropositivity cut-off for the assay was ≥ 5 EL.U/mL. Antibody concentrations below the cut-off of the assay were given an arbitrary value of half the cut-off for the purpose of GMC calculation. For this endpoint, the analysis was performed on the according-to-protocol cohort for immunogenicity, e. a., evaluable subjects for whom assay results were available for antibodies against at least one study vaccine antigen component after booster vaccination.

End point type	Secondary

End point timeframe:

Prior to (PRE) and one month (Month 1) post booster vaccination

End point values	Synflorix-Synflorix Group	Prevenar-Prevenar Group	Prevenar-Synflorix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	344	46	136	
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PT, PRE (N=332;34;133)	5.5 (5.1 to 6.1)	7.3 (5.2 to 10.3)	7 (6.1 to 8.1)	
Anti-PT, Month 1 (N=338;46;135)	79.6 (73.8 to 85.9)	76 (60.4 to 95.7)	85.8 (76.9 to 95.7)	
Anti-FHA, PRE (N=343;36;135)	27.1 (24.4 to 30.1)	29 (20.5 to 40.8)	35.5 (29.7 to 42.3)	
Anti-FHA, Month 1 (N=343;46;136)	357.7 (332.6 to 384.7)	334.5 (278.1 to 402.2)	400.2 (356.4 to 449.5)	
Anti-PRN, PRE (N=344;34;136)	9.1 (8.2 to 10.1)	11.1 (7.6 to 16.2)	12.1 (10.1 to 14.6)	
Anti-PRN, Month 1 (N=342;45;135)	248.9 (226.5 to 273.4)	204.6 (155.8 to 268.7)	276.5 (239.1 to 319.7)	

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-diphtheria (Anti-D) and anti-tetanus toxoids (Anti-TT) antibody concentrations

End point title	Anti-diphtheria (Anti-D) and anti-tetanus toxoids (Anti-TT) antibody concentrations

End point description:

Anti-D and Anti-TT antibody concentrations were calculated, expressed as geometric mean concentrations (GMCs), in International units per milliliter (IU/mL), and tabulated. The seropositivity cut-off for the assay was ≥ 0.1 IU/mL. Antibody concentrations below the cut-off of the assay were

given an arbitrary value of half the cut-off for the purpose of GMC calculation. For this endpoint, the analysis was performed on the according-to-protocol cohort for immunogenicity, e. a., evaluable subjects for whom assay results were available for antibodies against at least one study vaccine antigen component after booster vaccination.

End point type	Secondary

End point timeframe:

Prior to (PRE) and one month (Month 1) post booster vaccination

End point values	Synflorix-Synflorix Group	Prevenar-Prevenar Group	Prevenar-Synflorix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	344	46	136	
Units: IU/mL				
geometric mean (confidence interval 95%)				
Anti-D, PRE (N=344;34;136)	0.179 (0.161 to 0.199)	0.291 (0.2 to 0.424)	0.29 (0.25 to 0.336)	
Anti-D, Month 1 (N=343;45;136)	5.809 (5.352 to 6.305)	6.272 (4.883 to 8.055)	9.337 (8.419 to 10.356)	
Anti-TT, PRE (N=344;35;136)	0.417 (0.382 to 0.456)	0.261 (0.187 to 0.364)	0.265 (0.225 to 0.313)	
Anti-TT, Month 1 (N=343;46;136)	9.983 (9.293 to 10.724)	4.28 (3.294 to 5.562)	5.677 (5.038 to 6.397)	

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-hepatitis B surface antigen (HBs) antibody concentrations

End point title	Anti-hepatitis B surface antigen (HBs) antibody concentrations

End point description:

Anti-HBs antibody concentrations were calculated, expressed as geometric mean concentrations (GMCs), in milli-International unit per milliliter (mIU/mL), and tabulated. The seropositivity cut-off for the assay was ≥ 10 mIU/mL. Antibody concentrations below the cut-off of the assay were given an arbitrary value of half the cut-off for the purpose of GMC calculation. For this endpoint, the analysis was performed on the according-to-protocol cohort for immunogenicity, e. a., evaluable subjects for whom assay results were available for antibodies against at least one study vaccine antigen component after booster vaccination.

End point type	Secondary

End point timeframe:

Prior to (PRE) and one month (Month 1) post booster vaccination

End point values	Synflorix-Synflorix Group	Prevenar-Prevenar Group	Prevenar-Synflorix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	329	48	134	
Units: mIU/mL				
geometric mean (confidence interval 95%)				
Anti-HBs, PRE (N=329;48;134)	147.2 (124.7 to 173.7)	148.9 (100.4 to 220.8)	156.6 (125.5 to 195.5)	
Anti-HBs, Month 1 (N=325;47;132)	3869.1 (3218.1 to 4651.8)	3132.2 (1906.3 to 5146.5)	4358.6 (3495.5 to 5434.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-polio type 1, 2 and 3 (Anti-Polio 1, 2 and 3) antibody titers

End point title	Anti-polio type 1, 2 and 3 (Anti-Polio 1, 2 and 3) antibody titers

End point description:

Anti-Polio 1, 2 and 3 antibody titers were calculated, expressed as geometric mean titers (GMTs) and tabulated. The seroprotection cut-off for the assay was ≥ 8. Antibody titers below the cut-off of the assay were given an arbitrary value of half the cut-off for the purpose of GMT calculation. For this endpoint, the analysis was performed on the according-to-protocol cohort for immunogenicity, e. a., evaluable subjects for whom assay results were available for antibodies against at least one study vaccine antigen component after booster vaccination.

End point type	Secondary

End point timeframe:

Prior to (PRE) and one month (Month 1) post booster vaccination

End point values	Synflorix-Synflorix Group	Prevenar-Prevenar Group	Prevenar-Synflorix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	318	48	131	
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-Polio 1, PRE (N=318;48;131)	25.3 (21.9 to 29.3)	21.2 (15 to 30)	27.1 (20.7 to 35.4)	
Anti-Polio 1, Month 1 (N=279;42;121)	904.4 (779.7 to 1049.1)	819.3 (552.9 to 1214.2)	1003.7 (817.5 to 1232.3)	
Anti-Polio 2, PRE (N=317;46;130)	20.8 (18.1 to 24)	12.9 (8.8 to 18.9)	17.9 (14.1 to 22.8)	
Anti-Polio 2 , Month 1 (N=280;43;122)	793.5 (679.7 to 926.3)	495.7 (300.2 to 818.5)	661.2 (496.7 to 880.3)	
Anti-Polio 3, PRE (N=262;39;113)	33.7 (28.5 to 39.8)	25.8 (16.7 to 39.8)	28.2 (21.6 to 36.8)	
Anti-Polio 3, Month 1 (N=270;41;116)	1465 (1257.1 to 1707.3)	1191.7 (743.1 to 1911.3)	1646.5 (1294.4 to 2094.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects booster (BST) responder to pertussis toxoid (PT), filamentous haemagglutinin (FHA) and pertactin antigens

End point title	Number of subjects booster (BST) responder to pertussis toxoid (PT), filamentous haemagglutinin (FHA) and pertactin antigens

End point description:

A BST responder to PT, FHA and PRN antigens was defined as a subject with the appearance of antibodies in subjects who were seronegative prior to the booster vaccination or at least 2-fold increase of pre-booster vaccination antibody concentrations in subjects who were seropositive prior to the booster vaccination. A seropositive/seronegative subject as regards Anti-PT/-FHA/ -PRN antibodies was defined as a subject with anti-PT/-FHA/ -PRN antibody concentrations ≥ 5 Enzyme-linked Immunosorbent assay (ELISA) unit per milli-liter (EL.U/mL).

End point type	Secondary

End point timeframe:

One month (Month 1) post booster vaccination

End point values	Synflorix-Synflorix Group	Prevenar-Prevenar Group	Prevenar-Synflorix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	340	33	135	
Units: Subjects				
BST responder to PT antigens (N=324;31;132)	323	31	132	
BST responder to FHA antigens (N=340;33;135)	332	31	129	
BST responder to PRN antigens (N=340;31;135)	339	30	131	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Month 1 (Active Phase) and up to Month 6 (Extended Safety Follow-Up)

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	11.0

Reporting groups

Reporting group title	Prevenar-Prevenar Group

Reporting group description:

This group consisted of subjects previously vaccinated with the Prevenar vaccine as part of a previous study by GSK Biologicals – the 10PN-PD-DIT-001 (105553) study (EuDRA-CT number: 2005-003300-11). As part of the 105553 study, subjects had received a 3-dose primary vaccination of Prevenar vaccine at 2, 3 and 4 months of age (injected intramuscularly [IM] in the right thigh) co-administered with Infanrix hexa vaccine, except for the second dose in France, which was co-administered with Infanrix IPV Hib, injected intramuscularly in the left thigh. As part of this study, at 12-18 months of age, subjects received a booster dose of Prevenar vaccine, injected IM in the right thigh or deltoid, co-administered with Infanrix hexa vaccine, injected IM in the left thigh or deltoid.

Reporting group title	Prevenar-Synflorix Group

Reporting group description:

This group consisted of subjects previously vaccinated with the Prevenar vaccine as part of a previous study by GSK Biologicals – the 10PN-PD-DIT-001 (105553) study (EuDRA-CT number: 2005-003300-11). As part of the 105553 study, subjects had received a 3-dose primary vaccination of Synflorix vaccine at 2, 3 and 4 months of age (injected intramuscularly [IM] in the right thigh) co-administered with Infanrix hexa vaccine, except for the second dose in France, which was co-administered with Infanrix IPV Hib, injected intramuscularly in the left thigh. As part of this study, at 12-18 months of age, subjects received a booster dose of Synflorix, injected IM in the right thigh or deltoid, co-administered with Infanrix hexa vaccine, injected IM in the left thigh or deltoid.

Reporting group title	Synflorix-Synflorix Group

Reporting group description:

This group consisted of subjects previously vaccinated with the Synflorix vaccine as part of a previous study by GSK Biologicals – the 10PN-PD-DIT-001 (105553) study (EuDRA-CT number: 2005-003300-11). As part of the 105553 study, subjects had received a 3-dose primary vaccination of Synflorix vaccine at 2, 3 and 4 months of age (injected intramuscularly [IM] in the right thigh) co-administered with Infanrix hexa vaccine, except for the second dose in France, which was co-administered with Infanrix IPV Hib, injected intramuscularly in the left thigh. As part of this study, at 12-18 months of age, subjects received a booster dose of Synflorix vaccine, injected IM in the right thigh or deltoid, co-administered with Infanrix hexa vaccine, injected IM in the left thigh or deltoid.

Serious adverse events	Prevenar-Prevenar Group	Prevenar-Synflorix Group	Synflorix-Synflorix Group
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 92 (6.52%)	8 / 283 (2.83%)	33 / 737 (4.48%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Concussion	Additional description: SAE reported within the 31 days after the booster and during the ESFU, based on subjects participating for the ESFU phase.		
alternative dictionary used: MedDRA 11.0			

alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 92 (0.00%)	0 / 283 (0.00%)	1 / 737 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toxicity to various agents	Additional description: SAE reported within the 31 days after the booster and during the ESFU, based on subjects participating for the ESFU phase.		
alternative dictionary used: MedDRA 11.0			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 92 (0.00%)	0 / 283 (0.00%)	1 / 737 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Limb injury	Additional description: SAE reported within the 31 days after the booster and during the ESFU, based on subjects participating for the ESFU phase.		
alternative dictionary used: MedDRA 11.0			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 92 (0.00%)	0 / 283 (0.00%)	1 / 737 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thermal burn	Additional description: SAE reported within the 31 days after the booster and during the ESFU, based on subjects participating for the ESFU phase.		
alternative dictionary used: MedDRA 11.0			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 92 (1.09%)	0 / 283 (0.00%)	0 / 737 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Febrile convulsion	Additional description: SAE reported within the 31 days after the booster and during the ESFU, based on subjects participating for the ESFU phase.		
alternative dictionary used: MedDRA 11.0			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 92 (0.00%)	0 / 283 (0.00%)	2 / 737 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Microcytic anaemia	Additional description: SAE reported within the 31 days after the booster and during the ESFU, based on subjects participating for the ESFU phase.		
alternative dictionary used: MedDRA 11.0			

alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 92 (0.00%)	0 / 283 (0.00%)	1 / 737 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Peripheral swelling	Additional description: SAE reported within the 31 days after the booster and during the ESFU, based on subjects participating for the ESFU phase.		
alternative dictionary used: MedDRA 11.0			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 92 (0.00%)	1 / 283 (0.35%)	0 / 737 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Diarrhoea	Additional description: SAE reported within the 31 days after the booster and during the ESFU, based on subjects participating for the ESFU phase.		
alternative dictionary used: MedDRA 11.0			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 92 (1.09%)	0 / 283 (0.00%)	1 / 737 (0.14%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis	Additional description: SAE reported within the 31 days after the booster and during the ESFU, based on subjects participating for the ESFU phase.		
alternative dictionary used: MedDRA 11.0			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 92 (0.00%)	0 / 283 (0.00%)	1 / 737 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stomatitis	Additional description: SAE reported within the 31 days after the booster and during the ESFU, based on subjects participating for the ESFU phase.		
alternative dictionary used: MedDRA 11.0			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 92 (0.00%)	0 / 283 (0.00%)	1 / 737 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			

Asthma	Additional description: SAE reported within the 31 days after the booster and during the ESFU, based on subjects participating for the ESFU phase.		
alternative dictionary used: MedDRA 11.0			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 92 (0.00%)	0 / 283 (0.00%)	1 / 737 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis chronic	Additional description: SAE reported within the 31 days after the booster and during the ESFU, based on subjects participating for the ESFU phase.		
alternative dictionary used: MedDRA 11.0			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 92 (0.00%)	2 / 283 (0.71%)	6 / 737 (0.81%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Dermatitis atopic	Additional description: SAE reported within the 31 days after the booster and during the ESFU, based on subjects participating for the ESFU phase.		
alternative dictionary used: MedDRA 11.0			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 92 (0.00%)	0 / 283 (0.00%)	1 / 737 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Purpura	Additional description: SAE reported within the 31 days after the booster and during the ESFU, based on subjects participating for the ESFU phase.		
alternative dictionary used: MedDRA 11.0			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 92 (0.00%)	0 / 283 (0.00%)	1 / 737 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Adenovirus infection	Additional description: SAE reported within the 31 days after the booster and during the ESFU, based on subjects participating for the ESFU phase.		
alternative dictionary used: MedDRA 11.0			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 92 (0.00%)	0 / 283 (0.00%)	1 / 737 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Bronchiolitis	Additional description: SAE reported within the 31 days after the booster and during the ESFU, based on subjects participating for the ESFU phase.		
alternative dictionary used: MedDRA 11.0			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 92 (1.09%)	0 / 283 (0.00%)	0 / 737 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis	Additional description: SAE reported within the 31 days after the booster and during the ESFU, based on subjects participating for the ESFU phase.		
alternative dictionary used: MedDRA 11.0			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 92 (1.09%)	4 / 283 (1.41%)	2 / 737 (0.27%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear infection	Additional description: SAE reported within the 31 days after the booster and during the ESFU, based on subjects participating for the ESFU phase.		
alternative dictionary used: MedDRA 11.0			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 92 (1.09%)	0 / 283 (0.00%)	0 / 737 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis rotavirus	Additional description: SAE reported within the 31 days after the booster and during the ESFU, based on subjects participating for the ESFU phase.		
alternative dictionary used: MedDRA 11.0			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 92 (1.09%)	1 / 283 (0.35%)	1 / 737 (0.14%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngitis	Additional description: SAE reported within the 31 days after the booster and during the ESFU, based on subjects participating for the ESFU phase.		
alternative dictionary used: MedDRA 11.0			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 92 (2.17%)	0 / 283 (0.00%)	1 / 737 (0.14%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nasopharyngitis	Additional description: SAE reported within the 31 days after the booster and during the ESFU, based on subjects participating for the ESFU phase.		

alternative dictionary used: MedDRA 11.0			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 92 (0.00%)	1 / 283 (0.35%)	1 / 737 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media	Additional description: SAE reported within the 31 days after the booster and during the ESFU, based on subjects participating for the ESFU phase.		
alternative dictionary used: MedDRA 11.0			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 92 (0.00%)	1 / 283 (0.35%)	0 / 737 (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
Pharyngitis	Additional description: SAE reported within the 31 days after the booster and during the ESFU, based on subjects participating for the ESFU phase.		
alternative dictionary used: MedDRA 11.0			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 92 (0.00%)	0 / 283 (0.00%)	2 / 737 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia	Additional description: SAE reported within the 31 days after the booster and during the ESFU, based on subjects participating for the ESFU phase.		
alternative dictionary used: MedDRA 11.0			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 92 (0.00%)	0 / 283 (0.00%)	1 / 737 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis	Additional description: SAE reported within the 31 days after the booster and during the ESFU, based on subjects participating for the ESFU phase.		
alternative dictionary used: MedDRA 11.0			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 92 (0.00%)	0 / 283 (0.00%)	1 / 737 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection	Additional description: SAE reported within the 31 days after the booster and during the ESFU, based on subjects participating for the ESFU phase.		
alternative dictionary used: MedDRA 11.0			

alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 92 (0.00%)	0 / 283 (0.00%)	1 / 737 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection	Additional description: : SAE reported within the 31 days after the booster and during the ESFU, based on subjects participating for the ESFU phase.		
alternative dictionary used: MedDRA 11.0			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 92 (0.00%)	0 / 283 (0.00%)	1 / 737 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
alternative dictionary used: MedDRA 11.0			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 92 (0.00%)	1 / 283 (0.35%)	9 / 737 (1.22%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 9
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration	Additional description: SAE reported within the 31 days after the booster and during the ESFU, based on subjects participating for the ESFU phase.		
alternative dictionary used: MedDRA 11.0			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 92 (0.00%)	0 / 283 (0.00%)	1 / 737 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Weight gain poor	Additional description: SAE reported within the 31 days after the booster and during the ESFU, based on subjects participating for the ESFU phase.		
alternative dictionary used: MedDRA 11.0			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 92 (0.00%)	0 / 283 (0.00%)	1 / 737 (0.14%)
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: 4 %

Non-serious adverse events	Prevenar-Prevenar Group	Prevenar-Synflorix Group	Synflorix-Synflorix Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	85 / 92 (92.39%)	253 / 283 (89.40%)	684 / 737 (92.81%)
General disorders and administration site conditions			
Pain			
subjects affected / exposed	48 / 92 (52.17%)	150 / 283 (53.00%)	452 / 737 (61.33%)
occurrences (all)	48	150	452
Swelling			
subjects affected / exposed	42 / 92 (45.65%)	139 / 283 (49.12%)	338 / 737 (45.86%)
occurrences (all)	42	139	339
Somnolence			
subjects affected / exposed	48 / 92 (52.17%)	130 / 283 (45.94%)	303 / 737 (41.11%)
occurrences (all)	48	130	303
Pyrexia			
subjects affected / exposed	35 / 92 (38.04%)	118 / 283 (41.70%)	254 / 737 (34.46%)
occurrences (all)	36	124	254
Irritability			
subjects affected / exposed	55 / 92 (59.78%)	176 / 283 (62.19%)	438 / 737 (59.43%)
occurrences (all)	56	179	438
Decreased appetite			
subjects affected / exposed	31 / 92 (33.70%)	92 / 283 (32.51%)	230 / 737 (31.21%)
occurrences (all)	31	92	230
Injection site induration			
alternative assessment type: Non-systematic			
subjects affected / exposed	7 / 92 (7.61%)	7 / 283 (2.47%)	1 / 737 (0.14%)
occurrences (all)	7	7	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	3 / 92 (3.26%)	14 / 283 (4.95%)	7 / 737 (0.95%)
occurrences (all)	3	14	7
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	59 / 92 (64.13%)	153 / 283 (54.06%)	454 / 737 (61.60%)
occurrences (all)	59	154	454
Infections and infestations			

Rhinitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	4 / 92 (4.35%)	19 / 283 (6.71%)	28 / 737 (3.80%)
occurrences (all)	5	20	28
Upper respiratory tract infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	5 / 92 (5.43%)	13 / 283 (4.59%)	24 / 737 (3.26%)
occurrences (all)	6	13	24
Otitis media			
subjects affected / exposed	4 / 92 (4.35%)	11 / 283 (3.89%)	16 / 737 (2.17%)
occurrences (all)	6	12	17

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