Clinical trial results:
A phase III, randomized, open, controlled study in healthy Japanese children to assess the immunogenicity, safety and reactogenicity of GlaxoSmithKline Biologicals' 10-valent pneumococcal conjugate vaccine when co-administered with DTPa vaccine as a 3-dose primary immunization course at 3, 4 and 5 months of age and followed by a booster vaccination at 17-19 months of age.

Summary

EudraCT number	2011-003710-16
Trial protocol	Outside EU/EEA
Global end of trial date	17 September 2011

Results information

Result version number	v3 (current)
This version publication date	11 August 2022
First version publication date	29 July 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	112640

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01027845
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline K.K.
Sponsor organisation address	GSK Building - 6-15, Sendagaya 4-chome - Shibuya-ku, Tokyo , Japan, 151-8566
Public contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 44 2089904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 44 2089904466, GSKClinicalSupportHD@gsk.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000673-PIP01-09
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No	Yes

1901/2006 apply to this trial?	

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	07 May 2012
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 August 2010
Global end of trial reached?	Yes
Global end of trial date	17 September 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the immunogenicity of GSK Biologicals' 10-valent pneumococcal conjugate vaccine (10Pn-PD-DiT) in healthy Japanese children, one month post-dose 3, to the immune responses of the 10-valent pneumococcal conjugate vaccine as observed in the pivotal non-inferiority study 10PN-PD-DIT-001 (105553) in Europe.

Protection of trial subjects:

All subjects were supervised after vaccination with appropriate medical treatment readily available. Vaccines were administered by qualified and trained personnel. Only eligible subjects that had no contraindications to any components of the vaccines were vaccinated. Subjects were followed-up after each vaccination.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	08 December 2009
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Japan: 360
Worldwide total number of subjects	360
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	360
Children (2-11 years)	0

Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 360 subjects were enrolled in the study. All subjects received at least one vaccination dose.

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 trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	10Pn Group

Arm description:

Healthy male or female subjects, between 90 and 118 days of age who received, during primary vaccination phase, 3 doses of Synflorix (10Pn) vaccine, administered intramuscularly on alternating (left/right) sides of the anterolateral thigh and DPT "KAKETSUKEN" Syringe (DTPa) vaccine administered subcutaneously on alternating (left/right) sides of the distal one third of the upper arm. Both vaccines were administered at 3, 4, and 5 months of age, followed by a booster dose at 17-19 months of age (booster vaccination phase).

Arm type	Experimental
Investigational medicinal product name	Synflorix
Investigational medicinal product code	GSK1024850A
Other name	10Pn-PD-DiT, 10Pn, GlaxoSmithKline Biologicals' 10-valent pneumococcal polysaccharide and non-typeable Haemophilus influenzae protein D conjugate vaccine.
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 3 doses of 10Pn vaccine at 3, 4, and 5 months of age, followed by a booster dose at 17-19 months of age. The 10Pn vaccine was administered intramuscularly on alternating (left/right) sides of the anterolateral thigh.

Investigational medicinal product name	DPT "KAKETSUKEN" Syringe
Investigational medicinal product code	DTP
Other name	DTPa, Kaketsuken's adsorbed diphtheria-purified pertussis-tetanus combined vaccine.
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received 3 doses of DTPa vaccine at 3, 4, and 5 months of age, followed by a booster dose at 17-19 months of age. The DTPa vaccine was administered subcutaneously on alternating (left/right) sides of the upper arm.

Arm title	DTPa Group

Arm description:

Healthy male or female subjects, between 90 and 118 days of age, who received, during the primary vaccination phase, 3 doses of the DPT "KAKETSUKEN" Syringe (DTPa) vaccine, administered subcutaneously on alternating (left/right) sides of the distal one third of the upper arm at 3, 4, and 5 months of age, followed by a booster dose at 17-19 months of age (booster vaccination phase). Subjects from this group who also received at least one dose of Prevenar (PCV7): Pfizer's (formerly Wyeth Lederle) 7-valent pneumococcal conjugate vaccine, given before pre-booster blood sample (as

optional treatment considered as standard of care), were assigned to the DTPa + Prevenar Group in the booster phase, and subjects who did not receive any dose of Prevenar before pre-booster blood sample were assigned to the DTPa-no Prevenar Group in the booster phase. Some booster phase analyses were only performed on subjects of both pooled DTPa sub-groups, at the time of the analysis.

Arm type	Experimental
Investigational medicinal product name	DPT "KAKETSUKEN" Syringe
Investigational medicinal product code	DTP
Other name	DTPa, Kaketsuken's adsorbed diphtheria-purified pertussis-tetanus combined vaccine.
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subjects received 3 doses of DTPa vaccine at 3, 4, and 5 months of age, followed by a booster dose at 17-19 months of age. The DTPa vaccine was administered subcutaneously on alternating (left/right) sides of the upper arm.

Number of subjects in period 1	10Pn Group	DTPa Group
Started	237	123
Completed	226	120
Not completed	11	3
Adverse event, serious fatal	1	-
Consent withdrawn by subject	5	1
Adverse event, non-fatal	3	-
Protocol violation	1	-
Migrated/moved from study area	1	2

Baseline characteristics

Reporting groups	
Reporting group title	10Pn Group

Reporting group description:

Healthy male or female subjects, between 90 and 118 days of age who received, during primary vaccination phase, 3 doses of Synflorix (10Pn) vaccine, administered intramuscularly on alternating (left/right) sides of the anterolateral thigh and DPT "KAKETSUKEN" Syringe (DTPa) vaccine administered subcutaneously on alternating (left/right) sides of the distal one third of the upper arm. Both vaccines were administered at 3, 4, and 5 months of age, followed by a booster dose at 17-19 months of age (booster vaccination phase).

Reporting group title	DTPa Group

Reporting group description:

Healthy male or female subjects, between 90 and 118 days of age, who received, during the primary vaccination phase, 3 doses of the DPT "KAKETSUKEN" Syringe (DTPa) vaccine, administered subcutaneously on alternating (left/right) sides of the distal one third of the upper arm at 3, 4, and 5 months of age, followed by a booster dose at 17-19 months of age (booster vaccination phase). Subjects from this group who also received at least one dose of Prevenar (PCV7): Pfizer's (formerly Wyeth Lederle) 7-valent pneumococcal conjugate vaccine, given before pre-booster blood sample (as optional treatment considered as standard of care), were assigned to the DTPa + Prevenar Group in the booster phase, and subjects who did not receive any dose of Prevenar before pre-booster blood sample were assigned to the DTPa-no Prevenar Group in the booster phase. Some booster phase analyses were only performed on subjects of both pooled DTPa sub-groups, at the time of the analysis.

Reporting group values	10Pn Group	DTPa Group	Total
Number of subjects	237	123	360
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)	237	123	360
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: weeks			
arithmetic mean	13.6	13.5	
standard deviation	± 1.02	± 1.1	-
Gender categorical Units: Subjects			
Female	117	59	176
Male	120	64	184

Subject analysis sets	
Subject analysis set title	DTPa + Prevenar Group
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects from the DTPa Group with at least one dose of Prevenar (PCV7): Pfizer's (formerly Wyeth Lederle) 7-valent pneumococcal conjugate vaccine, given before prebooster blood sample and considered optional treatment as standard of care.

Subject analysis set title	DTPa - no Prevenar Group
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects from DTPa Group with no Prevenar vaccination before pre-booster blood sample.

Subject analysis set title	105553 10Pn Group
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Synflorix vaccine group (from 105553 study) that included subjects between 6 to 12 weeks of age at the time of the first vaccination with Synflorix, having received 3-dose primary vaccination course at 2-3-4 months of age of Synflorix (3 different lots) + Infanrix hexa (except for the second dose in France which was coadministered with Infanrix-IPV/Hib) vaccines. The number of subjects in this subject analysis set = 1107 subjects (360 being a placeholder value due to system constraint).

Reporting group values	DTPa + Prevenar Group	DTPa - no Prevenar Group	105553 10Pn Group
Number of subjects	119	1	360
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)	119	1	1107
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: weeks			
arithmetic mean			
standard deviation	±	±	±
Gender categorical Units: Subjects			
Female			
Male			

End points

End points reporting groups

Reporting group title	10Pn Group

Reporting group description:

Healthy male or female subjects, between 90 and 118 days of age who received, during primary vaccination phase, 3 doses of Synflorix (10Pn) vaccine, administered intramuscularly on alternating (left/right) sides of the anterolateral thigh and DPT "KAKETSUKEN" Syringe (DTPa) vaccine administered subcutaneously on alternating (left/right) sides of the distal one third of the upper arm. Both vaccines were administered at 3, 4, and 5 months of age, followed by a booster dose at 17-19 months of age (booster vaccination phase).

Reporting group title	DTPa Group

Reporting group description:

Healthy male or female subjects, between 90 and 118 days of age, who received, during the primary vaccination phase, 3 doses of the DPT "KAKETSUKEN" Syringe (DTPa) vaccine, administered subcutaneously on alternating (left/right) sides of the distal one third of the upper arm at 3, 4, and 5 months of age, followed by a booster dose at 17-19 months of age (booster vaccination phase). Subjects from this group who also received at least one dose of Prevenar (PCV7): Pfizer's (formerly Wyeth Lederle) 7-valent pneumococcal conjugate vaccine, given before pre-booster blood sample (as optional treatment considered as standard of care), were assigned to the DTPa + Prevenar Group in the booster phase, and subjects who did not receive any dose of Prevenar before pre-booster blood sample were assigned to the DTPa-no Prevenar Group in the booster phase. Some booster phase analyses were only performed on subjects of both pooled DTPa sub-groups, at the time of the analysis.

Subject analysis set title	DTPa + Prevenar Group
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects from the DTPa Group with at least one dose of Prevenar (PCV7): Pfizer's (formerly Wyeth Lederle) 7-valent pneumococcal conjugate vaccine, given before prebooster blood sample and considered optional treatment as standard of care.

Subject analysis set title	DTPa - no Prevenar Group
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects from DTPa Group with no Prevenar vaccination before pre-booster blood sample.

Subject analysis set title	105553 10Pn Group
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Synflorix vaccine group (from 105553 study) that included subjects between 6 to 12 weeks of age at the time of the first vaccination with Synflorix, having received 3-dose primary vaccination course at 2-3-4 months of age of Synflorix (3 different lots) + Infanrix hexa (except for the second dose in France which was coadministered with Infanrix-IPV/Hib) vaccines. The number of subjects in this subject analysis set = 1107 subjects (360 being a placeholder value due to system constraint).

Primary: Concentrations of Antibodies against Vaccine Pneumococcal Serotypes (primary immunization)

End point title	Concentrations of Antibodies against Vaccine Pneumococcal Serotypes (primary immunization)

End point description:

Concentrations were expressed as geometric mean concentrations (GMCs). Antibodies assessed for this outcome measure were those against the vaccine pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F (ANTI-1, -4, -5, -6B, -7F, -9V, -14, -18C, -19F and -23F). The seropositivity cut-off of the assay was an antibody concentration greater than or equal to (>=) 0.05 microgram per milliliter (µg/mL).

End point type	Primary

End point timeframe:

1 month following primary immunization (at Month 3)

End point values	10Pn Group	DTPa Group	105553 10Pn Group	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	231	121	1107	
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-1 (N=231, 119, 1100)	6.52 (5.85 to 7.26)	0.04 (0.03 to 0.04)	1.05 (1.00 to 1.10)	
Anti-4 (N=231, 120, 1106)	6.54 (5.86 to 7.30)	0.03 (0.03 to 0.03)	1.45 (1.38 to 1.53)	
Anti-5 (N=231, 119, 1104)	6.54 (5.94 to 7.21)	0.05 (0.04 to 0.06)	1.7 (1.62 to 1.78)	
Anti-6B (N=231, 121, 1100)	1.71 (1.43 to 2.05)	0.03 (0.03 to 0.03)	0.33 (0.30 to 0.36)	
Anti-7F (N=231, 120, 1107)	6.11 (5.50 to 6.78)	0.03 (0.03 to 0.04)	1.72 (1.64 to 1.80)	
Anti-9V (N=231, 119, 1103)	5.42 (4.81 to 6.10)	0.03 (0.03 to 0.03)	1.32 (1.25 to 1.38)	
Anti-14 (N=231, 120, 1100)	10.03 (8.80 to 11.43)	0.07 (0.06 to 0.09)	2.9 (2.75 to 3.05)	
Anti-18C (N=231, 121, 1102)	16.59 (14.40 to 19.13)	0.04 (0.03 to 0.04)	1.66 (1.56 to 1.77)	
Anti-19F (N=229, 118, 1104)	17.39 (15.53 to 19.48)	0.06 (0.05 to 0.07)	1.84 (1.71 to 1.98)	
Anti-23F (N=231, 119, 1102)	2.17 (1.83 to 2.57)	0.04 (0.03 to 0.04)	0.53 (0.50 to 0.57)	

Statistical analyses

Statistical analysis title	105553 10Pn over 10Pn- Anti-1 GMC ratio

Statistical analysis description:

At one month after primary immunization (post-dose 3), Enzyme-Linked Immunosorbent Assay (ELISA) Geometric Mean Concentration (GMC) ratios (105553 10Pn Group over 10Pn Group) were calculated for each of the 10 pneumococcal serotypes.

Comparison groups	10Pn Group v 105553 10Pn Group
Number of subjects included in analysis	1338
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Parameter estimate	GMC ratio
Point estimate	0.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.14
upper limit	0.18

Notes:

[1] - Comparability to the 105553 study in terms of non-inferiority was demonstrated if the upper limit (UL) of the two-sided 95% confidence interval (CI) on the GMC ratios (GMCs from 105553 10Pn Group over GMCs from 10Pn Group) was below a limit of 2-fold for all 10 vaccine pneumococcal serotypes.

Statistical analysis title	105553 10Pn over 10Pn- Anti-4 GMC ratio

Statistical analysis description:

At one month after primary immunization (post-dose 3), ELISA Geometric Mean Concentration (GMC) ratios (105553 10Pn Group over 10Pn Group) were calculated for each of the 10 pneumococcal serotypes.

Comparison groups	10Pn Group v 105553 10Pn Group
Number of subjects included in analysis	1338
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
Parameter estimate	GMC ratio
Point estimate	0.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.2
upper limit	0.25

Notes:

[2] - Comparability to the 105553 study in terms of non-inferiority was demonstrated if the upper limit (UL) of the two-sided 95% confidence interval (CI) on the GMC ratios (GMCs from 105553 10Pn Group over GMCs from 10Pn Group) was below a limit of 2-fold for all 10 vaccine pneumococcal serotypes.

Statistical analysis title	105553 10Pn over 10Pn- Anti-5 GMC ratio

Statistical analysis description:

At one month after primary immunization (post-dose 3), ELISA Geometric Mean Concentration (GMC) ratios (105553 10Pn Group over 10Pn Group) were calculated for each of the 10 pneumococcal serotypes.

Comparison groups	10Pn Group v 105553 10Pn Group
Number of subjects included in analysis	1338
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
Parameter estimate	GMC ratio
Point estimate	0.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.23
upper limit	0.29

Notes:

[3] - Comparability to the 105553 study in terms of non-inferiority was demonstrated if the upper limit (UL) of the two-sided 95% confidence interval (CI) on the GMC ratios (GMCs from 105553 10Pn Group over GMCs from 10Pn Group) was below a limit of 2-fold for all 10 vaccine pneumococcal serotypes.

Statistical analysis title	105553 10Pn over 10Pn- Anti-6B GMC ratio

Statistical analysis description:

At one month after primary immunization (post-dose 3), ELISA Geometric Mean Concentration (GMC) ratios (105553 10Pn Group over 10Pn Group) were calculated for each of the 10 pneumococcal serotypes.

Comparison groups	10Pn Group v 105553 10Pn Group
Number of subjects included in analysis	1338
Analysis specification	Pre-specified
Analysis type	non-inferiority[4]
Parameter estimate	GMC ratio
Point estimate	0.19

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.16
upper limit	0.23

Notes:

[4] - Comparability to the 105553 study in terms of non-inferiority was demonstrated if the upper limit (UL) of the two-sided 95% confidence interval (CI) on the GMC ratios (GMCs from 105553 10Pn Group over GMCs from 10Pn Group) was below a limit of 2-fold for all 10 vaccine pneumococcal serotypes.

Statistical analysis title	105553 10Pn over 10Pn- Anti-7F GMC ratio

Statistical analysis description:

At one month after primary immunization (post-dose 3), ELISA Geometric Mean Concentration (GMC) ratios (105553 10Pn Group over 10Pn Group) were calculated for each of the 10 pneumococcal serotypes.

Comparison groups	10Pn Group v 105553 10Pn Group
Number of subjects included in analysis	1338
Analysis specification	Pre-specified
Analysis type	non-inferiority[5]
Parameter estimate	GMC ratio
Point estimate	0.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.25
upper limit	0.31

Notes:

[5] - Comparability to the 105553 study in terms of non-inferiority was demonstrated if the upper limit (UL) of the two-sided 95% confidence interval (CI) on the GMC ratios (GMCs from 105553 10Pn Group over GMCs from 10Pn Group) was below a limit of 2-fold for all 10 vaccine pneumococcal serotypes.

Statistical analysis title	105553 10Pn over 10Pn- Anti-9V GMC ratio

Statistical analysis description:

At one month after primary immunization (post-dose 3), ELISA Geometric Mean Concentration (GMC) ratios (105553 10Pn Group over 10Pn Group) were calculated for each of the 10 pneumococcal serotypes.

Comparison groups	10Pn Group v 105553 10Pn Group
Number of subjects included in analysis	1338
Analysis specification	Pre-specified
Analysis type	non-inferiority[6]
Parameter estimate	GMC ratio
Point estimate	0.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.22
upper limit	0.27

Notes:

[6] - Comparability to the 105553 study in terms of non-inferiority was demonstrated if the upper limit (UL) of the two-sided 95% confidence interval (CI) on the GMC ratios (GMCs from 105553 10Pn Group over GMCs from 10Pn Group) was below a limit of 2-fold for all 10 vaccine pneumococcal serotypes.

Statistical analysis title	105553 10Pn over 10Pn- Anti-14 GMC ratio

Statistical analysis description:

At one month after primary immunization (post-dose 3), ELISA Geometric Mean Concentration (GMC) ratios (105553 10Pn Group over 10Pn Group) were calculated for each of the 10 pneumococcal

serotypes.

Comparison groups	10Pn Group v 105553 10Pn Group
Number of subjects included in analysis	1338
Analysis specification	Pre-specified
Analysis type	non-inferiority[7]
Parameter estimate	GMC ratio
Point estimate	0.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.25
upper limit	0.33

Notes:

[7] - Comparability to the 105553 study in terms of non-inferiority was demonstrated if the upper limit (UL) of the two-sided 95% confidence interval (CI) on the GMC ratios (GMCs from 105553 10Pn Group over GMCs from 10Pn Group) was below a limit of 2-fold for all 10 vaccine pneumococcal serotypes.

Statistical analysis title	105553 10Pn over 10Pn- Anti-18C GMC ratio

Statistical analysis description:

At one month after primary immunization (post-dose 3), ELISA Geometric Mean Concentration (GMC) ratios (105553 10Pn Group over 10Pn Group) were calculated for each of the 10 pneumococcal serotypes.

Comparison groups	10Pn Group v 105553 10Pn Group
Number of subjects included in analysis	1338
Analysis specification	Pre-specified
Analysis type	non-inferiority[8]
Parameter estimate	GMC ratio
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.09
upper limit	0.12

Notes:

[8] - Comparability to the 105553 study in terms of non-inferiority was demonstrated if the upper limit (UL) of the two-sided 95% confidence interval (CI) on the GMC ratios (GMCs from 105553 10Pn Group over GMCs from 10Pn Group) was below a limit of 2-fold for all 10 vaccine pneumococcal serotypes.

Statistical analysis title	105553 10Pn over 10Pn- Anti-19F GMC ratio

Statistical analysis description:

At one month after primary immunization (post-dose 3), ELISA Geometric Mean Concentration (GMC) ratios (105553 10Pn Group over 10Pn Group) were calculated for each of the 10 pneumococcal serotypes.

Comparison groups	10Pn Group v 105553 10Pn Group
Number of subjects included in analysis	1338
Analysis specification	Pre-specified
Analysis type	non-inferiority[9]
Parameter estimate	GMC ratio
Point estimate	0.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.09
upper limit	0.12

Notes:

[9] - Comparability to the 105553 study in terms of non-inferiority was demonstrated if the upper limit (UL) of the two-sided 95% confidence interval (CI) on the GMC ratios (GMCs from 105553 10Pn Group over GMCs from 10Pn Group) was below a limit of 2-fold for all 10 vaccine pneumococcal serotypes.

Statistical analysis title	105553 10Pn over 10Pn- Anti-23F GMC ratio

Statistical analysis description:

At one month after primary immunization (post-dose 3), ELISA Geometric Mean Concentration (GMC) ratios (105553 10Pn Group over 10Pn Group) were calculated for each of the 10 pneumococcal serotypes.

Comparison groups	10Pn Group v 105553 10Pn Group
Number of subjects included in analysis	1338
Analysis specification	Pre-specified
Analysis type	non-inferiority[10]
Parameter estimate	GMC ratio
Point estimate	0.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.21
upper limit	0.29

Notes:

[10] - Comparability to the 105553 study in terms of non-inferiority was demonstrated if the upper limit (UL) of the two-sided 95% confidence interval (CI) on the GMC ratios (GMCs from 105553 10Pn Group over GMCs from 10Pn Group) was below a limit of 2-fold for all 10 vaccine pneumococcal serotypes.

Secondary: Concentrations of Antibodies against Vaccine Pneumococcal Serotypes (booster immunization)

End point title	Concentrations of Antibodies against Vaccine Pneumococcal Serotypes (booster immunization)[11]

End point description:

Antibodies assessed were those against the vaccine pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F (ANTI-1, -4, -5, -6B, -7F, -9V, -14, -18C, -19F and -23F). Antibody concentrations were measured by 22F ELISA, expressed as GMCs, in µg/mL. The seropositivity cut-off of the assay was an antibody concentration >= 0.05 µg/mL. Antibody concentrations <0.05 µg/mL were given an arbitrary value of half the cut-off for the purpose of GMC calculation. Administration of catch-up pneumococcal vaccination with a licensed product other than Synflorix was allowed in the DTPa Group at least 7 days before DTPa vaccine booster dose. Thus, for this booster phase analysis, the DTPa Group was further split in DTPa + Prevenar Group and DTPa - no Prevenar Group. Lower and Upper Limits of the 95% confidence interval could not be calculated in the DTPa - no Prevenar Group because number of subjects affected = 0: both limits have been entered = to GMC value (system constraint workaround).

End point type	Secondary

End point timeframe:

Prior to (PRE, at Month 14-16) and one month after booster (POST, at Month 15-17) immunization

Notes:

[11] - 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 participants from the 10Pn Group, the DTPa + Prevenar Group and the DTPa - no Prevenar Group.

End point values	10Pn Group	DTPa + Prevenar Group	DTPa - no Prevenar Group	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	216	114	1	
Units: µg/mL				
geometric mean (confidence interval 95%)				

Anti-1 PRE (N=216,113,1)	0.8 (0.69 to 0.92)	0.04 (0.03 to 0.04)	0.03 (-99999 to 99999)	
Anti-1 POST (N=214,114,1)	7.81 (6.91 to 8.82)	0.04 (0.04 to 0.05)	0.24 (-99999 to 99999)	
Anti-4 PRE (N=215,114,1)	0.81 (0.7 to 0.93)	0.85 (0.71 to 1.02)	0.03 (-99999 to 99999)	
Anti-4 POST (N=213,114,1)	12.89 (11.41 to 14.56)	0.78 (0.64 to 0.94)	0.03 (-99999 to 99999)	
Anti-5 PRE (N=216,114,1)	1.22 (1.05 to 1.41)	0.08 (0.07 to 0.1)	0.05 (-99999 to 99999)	
Anti-5 POST (N=214,114,1)	8.81 (7.87 to 9.86)	0.15 (0.12 to 0.17)	0.03 (-99999 to 99999)	
Anti-6B PRE (N=215,114,1)	0.93 (0.79 to 1.1)	0.34 (0.27 to 0.44)	0.03 (-99999 to 99999)	
Anti-6B POST (N=214,114,1)	3.66 (3.14 to 4.27)	0.33 (0.25 to 0.42)	0.03 (-99999 to 99999)	
Anti-7F PRE (N=215,114,1)	1.48 (1.32 to 1.65)	0.05 (0.04 to 0.05)	0.03 (-99999 to 99999)	
Anti-7F POST (N=214,114,1)	10.68 (9.66 to 11.81)	0.09 (0.08 to 0.11)	0.03 (-99999 to 99999)	
Anti-9V PRE (N=212,114,1)	1.81 (1.61 to 2.03)	1.01 (0.83 to 1.25)	0.03 (-99999 to 99999)	
Anti-9V POST (N=214,114,1)	12.79 (11.49 to 14.23)	0.96 (0.79 to 1.17)	0.03 (-99999 to 99999)	
Anti-14 PRE (N=216,114,1)	2.37 (2.04 to 2.74)	3.17 (2.74 to 3.67)	0.09 (-99999 to 99999)	
Anti-14 POST (N=214,114,1)	15.72 (13.97 to 17.69)	2.92 (2.53 to 3.38)	0.16 (-99999 to 99999)	
Anti-18C PRE (N=215,114,1)	2.18 (1.89 to 2.51)	0.94 (0.79 to 1.11)	0.03 (-99999 to 99999)	
Anti-18C POST (N=213,114,1)	34.9 (31.05 to 39.23)	0.77 (0.65 to 0.92)	0.03 (-99999 to 99999)	
Anti-19F PRE (N=215,114,1)	2.92 (2.5 to 3.41)	0.51 (0.38 to 0.68)	0.03 (-99999 to 99999)	
Anti-19F POST (N=214,114,1)	28.72 (25.29 to 32.63)	0.68 (0.51 to 0.91)	0.03 (-99999 to 99999)	
Anti-23F PRE (N=213,114,1)	1.14 (0.93 to 1.39)	0.55 (0.42 to 0.73)	0.03 (-99999 to 99999)	
Anti-23F POST (N=214,114,1)	7.68 (6.68 to 8.83)	0.88 (0.7 to 1.12)	0.03 (-99999 to 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Opsonophagocytic Titers against Vaccine Pneumococcal Serotypes (primary immunization)

End point title	Opsonophagocytic Titers against Vaccine Pneumococcal Serotypes (primary immunization)

End point description:

Pneumococcal vaccine serotypes assessed were 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F and were calculated, expressed as geometric mean titers (GMTs). The seropositivity cut-off for the assay was >= 8. Antibody titers < 8 were given an arbitrary value of half the cut-off for the purpose of GMT calculation.

End point type	Secondary

End point timeframe:

1 month following primary immunization (at Month 3)

End point values	10Pn Group	DTPa Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	224	116		
Units: Titer				
geometric mean (confidence interval 95%)				
OPSONO-1 (N=223,115)	619.8 (511.9 to 750.6)	4.8 (4.2 to 5.5)		
OPSONO-4 (N=221,115)	1184.6 (1043.7 to 1344.5)	4.1 (3.9 to 4.3)		
OPSONO-5 (N=224,115)	335.1 (286.4 to 392.1)	4.2 (4 to 4.5)		
OPSONO-6B (N=222,116)	1926.6 (1559.6 to 2380)	5 (4.2 to 5.9)		
OPSONO-7F (N=216,108)	7905.9 (6854.5 to 9118.6)	69.5 (43.2 to 111.9)		
OPSONO-9V (N=219,108)	4063.4 (3565.8 to 4630.4)	4.9 (4.2 to 5.6)		
OPSONO-14 (N=217,103)	3392.4 (2962.5 to 3884.8)	6.5 (5 to 8.5)		
OPSONO-18C (N=217,108)	893.2 (727.7 to 1096.2)	4.8 (4 to 5.7)		
OPSONO-19F (N=219,115)	1254.6 (1031.1 to 1526.5)	4.4 (4 to 4.9)		
OPSONO-23F (N=218,107)	4312.1 (3401.5 to 5466.5)	6 (4.5 to 8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of Antibodies against Cross-reactive Pneumococcal Serotypes 6A and 19A (primary immunization)

End point title	Concentrations of Antibodies against Cross-reactive Pneumococcal Serotypes 6A and 19A (primary immunization)

End point description:

Concentrations were given in µg/mL and were expressed in geometric mean antibody concentrations. Cross-reactive pneumococcal vaccine serotypes assessed were 6A and 19A. The seropositivity cut-off of the assay was an antibody concentration >= 0.05 µg/mL. Antibody concentrations < 0.05 µg/mL were given an arbitrary value of half the cut-off for the purpose of GMC calculation.

End point type	Secondary

End point timeframe:

1 month following primary immunization (at Month 3)

End point values	10Pn Group	DTPa Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	231	121		
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-6A (N=230,121)	0.41 (0.34 to 0.49)	0.04 (0.03 to 0.04)		
Anti-19A (N=231,121)	0.48 (0.4 to 0.57)	0.04 (0.04 to 0.05)		

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of Antibodies Against Cross-reactive Pneumococcal Serotypes 6A and 19A (booster immunization)

End point title	Concentrations of Antibodies Against Cross-reactive Pneumococcal Serotypes 6A and 19A (booster immunization)[12]

End point description:

Concentrations were given in µg/mL and were expressed in geometric mean antibody concentrations. Cross-reactive pneumococcal vaccine serotypes assessed were 6A and 19A. The seropositivity cut-off of the assay was an antibody concentration >= 0.05 µg/mL. Antibody concentrations < 0.05 g/mL were given an arbitrary value of half the cut-off for the purpose of GMC calculation. Administration of catch-up pneumococcal vaccination with a licensed product other than Synflorix was allowed in the DTPa Group at least 7 days before DTPa vaccine booster dose. Thus, for this booster phase analysis, the DTPa Group was further split in DTPa + Prevenar Group and DTPa - no Prevenar Group. Lower and Upper Limits of the 95% confidence interval could not be calculated in the DTPa - no Prevenar Group because number of subjects affected = 0: both limits have been entered = to GMC value (system constraint workaround).

End point type	Secondary

End point timeframe:

Prior to (PRE, at Month 14-16) and one month after booster (POST, at Month 15-17) immunization

Notes:

[12] - 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 participants from the 10Pn Group, the DTPa + Prevenar Group and the DTPa - no Prevenar Group.

End point values	10Pn Group	DTPa + Prevenar Group	DTPa - no Prevenar Group	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	214	114	1	
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-6A PRE (N=209,114,1)	0.61 (0.5 to 0.75)	0.19 (0.14 to 0.26)	0.03 (-99999 to 99999)	

Anti-6A POST (N=214,114,1)	2.72 (2.24 to 3.3)	0.21 (0.16 to 0.27)	0.03 (-99999 to 99999)	
Anti-19A PRE (N=214,114,1)	0.57 (0.45 to 0.71)	0.12 (0.09 to 0.16)	0.03 (-99999 to 99999)	
Anti-19A POST (N=214,114,1)	5.16 (4.18 to 6.37)	0.15 (0.11 to 0.2)	0.03 (-99999 to 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Opsonophagocytic Titers against Cross-reactive Pneumococcal Serotypes 6A and 19A (primary immunization)

End point title	Opsonophagocytic Titers against Cross-reactive Pneumococcal Serotypes 6A and 19A (primary immunization)

End point description:

Cross-reactive pneumococcal vaccine serotypes assessed were 6A and 19A and were calculated, expressed as GMTs. The seropositivity cut-off for the assay was >= 8. Antibody titers < 8 were given an arbitrary value of half the cut-off for the purpose of GMT calculation.

End point type	Secondary

End point timeframe:

1 month following primary immunization (at Month 3)

End point values	10Pn Group	DTPa Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	213	115		
Units: Titer				
geometric mean (confidence interval 95%)				
Opsono-6A (N=206,106)	339.6 (253.8 to 454.4)	4.6 (4.1 to 5.1)		
Opsono-19A (N=213,115)	34.3 (26.2 to 44.9)	4.3 (4 to 4.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Opsonophagocytic Titers against Cross-reactive Pneumococcal Serotypes 6A and 19A (booster immunization)

End point title	Opsonophagocytic Titers against Cross-reactive Pneumococcal Serotypes 6A and 19A (booster immunization)[13]

End point description:

Cross-reactive pneumococcal vaccine serotypes assessed were 6A and 19A and were calculated, expressed as GMTs. The seropositivity cut-off for the assay was >= 8. Antibody titers < 8 were given an arbitrary value of half the cut-off for the purpose of GMT calculation. Administration of catch-up pneumococcal vaccination with a licensed product other than Synflorix was allowed in the DTPa Group at least 7 days before DTPa vaccine booster dose. Thus, for this booster phase analysis, the DTPa Group

was further split in DTPa + Prevenar Group and DTPa - no Prevenar Group. Lower and Upper Limits of the 95% confidence interval could not be calculated in the DTPa - no Prevenar Group because number of subjects affected = 0: both limits have been entered = to GMC value (system constraint workaround).

End point type	Secondary

End point timeframe:

Prior to (PRE, at Month 14-16) and one month after booster (POST, at Month 15-17) immunization

Notes:

[13] - 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 participants from the 10Pn Group, the DTPa + Prevenar Group and the DTPa - no Prevenar Group.

End point values	10Pn Group	DTPa + Prevenar Group	DTPa - no Prevenar Group	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	213	111	1	
Units: Titer				
geometric mean (confidence interval 95%)				
OPSONO-6A PRE (N=196,107,1)	138.5 (103.3 to 185.7)	60.4 (35.2 to 103.7)	4 (-99999 to 99999)	
OPSONO-6A POST (N=212,107,1)	767.9 (593.1 to 994.1)	103.3 (60.4 to 176.6)	4 (-99999 to 99999)	
OPSONO-19A PRE (N=213,111,1)	13.1 (10.1 to 16.9)	7.7 (5.5 to 10.6)	4 (-99999 to 99999)	
OPSONO-19A POST (N=212,109,1)	431.4 (330.9 to 562.4)	8.6 (6 to 12.2)	4 (-99999 to 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of Antibodies against Protein D (PD) (primary immunization)

End point title	Concentrations of Antibodies against Protein D (PD) (primary immunization)

End point description:

Anti-protein D (Anti-PD) antibody concentrations by ELISA were calculated, expressed as 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 < 100 EL.U/mL were given an arbitrary value of half the cut-off for the purpose of GMC calculation.

End point type	Secondary

End point timeframe:

1 month following primary immunization (at Month 3)

End point values	10Pn Group	DTPa Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	229	119		
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PD	2548.6 (2315.1 to 2805.7)	87.9 (75.8 to 102)		

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of Anti-PD (booster immunization)

End point title	Concentrations of Anti-PD (booster immunization)

End point description:

Anti-PD antibody concentrations by ELISA were calculated, expressed as GMCs)in ELISA EL.U/mL and tabulated. The seropositivity cut-off for the assay was >= 100 EL.U/mL. Antibody concentrations < 100 EL.U/mL were given an arbitrary value of half the cut-off for the purpose of GMC calculation. The DTPa Group, at the time of the booster immunization, include subjects with or without Prevenar vaccination administered before the booster dose.

End point type	Secondary

End point timeframe:

Prior to (PRE, at Month 14-16) and one month after booster (POST, at Month 15-17) immunization

End point values	10Pn Group	DTPa Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	214	113		
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PD PRE (N=210,112)	702.6 (601 to 821.5)	82.3 (71.7 to 94.5)		
Anti-PD POST (N=214,113)	2916.9 (2552.9 to 3332.7)	86.9 (75.1 to 100.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of Antibodies Against Diphtheria Toxoid (DT) and Tetanus Toxoid (TT) (primary immunization)

End point title	Concentrations of Antibodies Against Diphtheria Toxoid (DT) and Tetanus Toxoid (TT) (primary immunization)

End point description:

Concentrations of antibodies are presented as GMCs expressed as International units per millilitre (IU/mL). Seroprotection status, defined as Anti-DT or Anti-TT antibody concentration equal to or greater than 0.1 IU/mL.

End point type	Secondary

End point timeframe:

1 month following primary immunization (at Month 3)

End point values	10Pn Group	DTPa Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	230	120		
Units: IU/mL				
geometric mean (confidence interval 95%)				
Anti-DT (N=229,120)	5.363 (5.002 to 5.749)	3.829 (3.464 to 4.233)		
Anti-TT (N=230,120)	5.427 (4.94 to 5.962)	3.626 (3.174 to 4.143)		

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of Anti-DT and Anti-TT (booster immunization)

End point title	Concentrations of Anti-DT and Anti-TT (booster immunization)

End point description:

Concentrations of antibodies are presented as geometric mean concentrations expressed as IU/mL. Seroprotection status, defined as Anti-DT or Anti-TT antibody concentration >= 0.1 IU/mL. The DTPa Group, at the time of the booster immunization, included subjects with or without Prevenar vaccination administered before the booster dose.

End point type	Secondary

End point timeframe:

Prior to (PRE, at Month 14-16) and one month after booster (POST, at Month 15-17) immunization

End point values	10Pn Group	DTPa Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	226	119		
Units: IU/mL				
geometric mean (confidence interval 95%)				
Anti-DT PRE (N=219,118)	0.625 (0.564 to 0.692)	0.707 (0.611 to 0.817)		
Anti-DT POST (N=226,119)	15.324 (13.965 to 16.815)	10.587 (9.470 to 11.834)		
Anti-TT PRE (N=221,116)	2.007 (1.662 to 2.424)	1.328 (1.029 to 1.715)		

Anti-TT POST (N=226,119)	10.724 (9.664 to 11.901)	6.059 (5.160 to 7.114)		

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of Antibodies against pertussis (PT) and filamentous haemagglutinin (FHA) (primary immunization)

End point title	Concentrations of Antibodies against pertussis (PT) and filamentous haemagglutinin (FHA) (primary immunization)

End point description:

Concentrations of antibodies are presented as GMCs expressed as ELISA EL.U/mL. Seropositivity was defined as an antibody concentration equal to or greater than 5 EL.U/mL.

End point type	Secondary

End point timeframe:

1 month following primary immunization (at Month 3)

End point values	10Pn Group	DTPa Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	231	121		
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PT	123.2 (115.2 to 131.7)	133.1 (119.5 to 148.3)		
Anti-FHA	308.6 (284.8 to 334.3)	365 (327.9 to 406.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of Anti-PT and FHA (booster immunization)

End point title	Concentrations of Anti-PT and FHA (booster immunization)

End point description:

Concentrations of antibodies are presented as geometric mean concentrations expressed as ELISA EL.U/mL. Seropositivity was defined as an antibody concentration equal to or greater than 5 EL.U/mL. The DTPa Group, at the time of the booster immunization, include subjects with or without Prevenar vaccination administered before the booster dose.

End point type	Secondary

End point timeframe:

Prior to (PRE, at Month 14-16) and one month after booster (POST, at Month 15-17) immunization

End point values	10Pn Group	DTPa Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	214	114		
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PT PRE (N=210,113)	14.9 (13.2 to 16.8)	18.1 (15.1 to 21.7)		
Anti-PT POST (N=213,114)	158.4 (143.7 to 174.7)	204 (176.7 to 235.6)		
Anti-FHA PRE (N=210,114)	37.9 (33.3 to 43.1)	48.4 (40.6 to 57.8)		
Anti-FHA POST (N=214,113)	460.6 (421.2 to 503.7)	584.5 (512.6 to 666.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Any and Grade 3 Solicited Local Symptoms after Primary Vaccination

End point title	Number of Subjects With Any and Grade 3 Solicited Local Symptoms after Primary Vaccination

End point description:

Solicited local AEs assessed were pain, redness and swelling. Any = incidence of any local symptom regardless of intensity grade. Grade 3 pain = cried when limb was moved/spontaneously painful. Grade 3 redness/swelling = redness/swelling above 30 millimetre.

End point type	Secondary

End point timeframe:

During the 8-day (Days 0-7) after each primary vaccine dose

End point values	10Pn Group	DTPa Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	237	123		
Units: Subjects				
Any pain Dose 1 (N=237,123)	83	19		
Grade 3 pain Dose 1 (N=237,123)	1	0		
Any redness Dose 1 (N=237,123)	182	71		
Grade 3 Redness Dose 1 (N=237,123)	10	0		
Any swelling Dose 1 (N=237,123)	126	33		
Grade 3 Swelling Dose 1 (N=237,123)	16	0		
Any pain Dose 2 (N=235,123)	74	26		
Grade 3 pain Dose 2 (N=235,123)	0	0		
Any redness Dose 2 (N=235,123)	200	96		
Grade 3 Redness Dose 2 (N=235,123)	25	4		

Any swelling Dose 2 (N=235,123)	160	75		
Grade 3 Swelling Dose 2 (N=235,123)	26	4		
Any pain Dose 3 (N=233,122)	63	23		
Grade 3 pain Dose 3 (N=233,122)	1	0		
Any redness Dose 3 (N=233,122)	178	84		
Grade 3 Redness Dose 3 (N=233,122)	24	0		
Any swelling Dose 3 (N=233,122)	142	65		
Grade 3 Swelling Dose 3 (N=233,122)	27	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Any, Grade 3 and Related Solicited General Symptoms after Primary Vaccination

End point title	Number of Subjects with Any, Grade 3 and Related Solicited General Symptoms after Primary Vaccination

End point description:

General AEs = drowsiness, fever (axillary >= 37.5 degrees Celsius), irritabilityand loss of appetite, vomiting. Any= Incidence of any symptom regardless of intensity grade or relationship to vaccination. Grade 3: drowsiness = prevented normal activity. Grade 3 irritability = crying that could not be comforted/ prevented normal activity. Grade 3 loss of appetite = not eating at all. Grade 3 fever = greater than (>) 39.5°C Related = symptom assessed by the investigator as related to the vaccination.

End point type	Secondary

End point timeframe:

During the 8-day (Days 0-7) after each primary vaccine dose

End point values	10Pn Group	DTPa Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	237	123		
Units: Subjects				
Any drowsiness Dose 1 (N=237,123)	67	24		
Grade 3 drowsiness Dose 1 (N=237,123)	3	0		
Related drowsiness Dose 1 (N=237,123)	24	6		
Any Fever Dose 1 (N=237,123)	61	20		
Grade 3 Fever Dose 1 (N=237,123)	1	0		
Related fever Dose 1 (N=237,123)	20	5		
Any irritability Dose 1 (N=237,123)	100	43		
Grade 3 irritability Dose 1 (N=237,123)	6	3		
Related irritability Dose 1 (N=237,123)	40	12		
Any loss of appetite Dose 1 (N=237,123)	32	12		
Grade 3 loss of appetite Dose 1 (N=237,123)	0	0		
Related loss of appetite Dose 1 (N=237,123)	4	1		
Any drowsiness Dose 2 (N=235,123)	67	34		

Grade 3 drowsiness Dose 2 (N=235,123)	2	0		
Related drowsiness Dose 2 (N=235,123)	26	9		
Any Fever Dose 2 (N=235,123)	65	22		
Grade 3 Fever Dose 2 (N=235,123)	0	0		
Related fever Dose 2 (N=235,123)	31	7		
Any irritability Dose 2 (N=235,123)	88	45		
Grade 3 irritability Dose 2 (N=235,123)	4	0		
Related irritability Dose 2 (N=235,123)	30	12		
Any loss of appetite Dose 2 (N=235,123)	27	7		
Grade 3 loss of appetite Dose 2 (N=235,123)	0	0		
Related loss of appetite Dose 2 (N=235,123)	7	2		
Any drowsiness Dose 3 (N=233,122)	41	25		
Grade 3 drowsiness Dose 3 (N=233,122)	0	0		
Related drowsiness Dose 3 (N=233,122)	15	10		
Any Fever Dose 3 (N=233,122)	51	21		
Grade 3 Fever Dose 3 (N=233,122)	2	0		
Related fever Dose 3 (N=233,122)	21	2		
Any irritability Dose 3 (N=233,122)	80	31		
Grade 3 irritability Dose 3 (N=233,122)	3	0		
Related irritability Dose 3 (N=233,122)	31	10		
Any loss of appetite Dose 3 (N=233,122)	25	7		
Grade 3 loss of appetite Dose 3 (N=233,122)	0	0		
Related loss of appetite Dose 3 (N=233,122)	5	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Any and Grade 3 Solicited Local Symptoms after Booster Vaccination

End point title	Number of Subjects With Any and Grade 3 Solicited Local Symptoms after Booster Vaccination

End point description:

Solicited local AEs assessed were pain, redness and swelling. Any = incidence of any local symptom regardless of intensity grade. Grade 3 pain = cried when limb was moved/spontaneously painful. Grade 3 redness/swelling = redness/swelling above 30 millimetres. The DTPa Group, at the time of the booster immunization, include subjects with or without Prevenar vaccination administered before the booster dose.

End point type	Secondary

End point timeframe:

During the 8-day (Days 0-7) period following booster vaccination

End point values	10Pn Group	DTPa Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	228	120		
Units: Subjects				
Any pain	134	47		
Grade 3 pain	12	0		
Any redness	197	102		
Redness > 30 mm	72	20		
Any swelling	180	90		
Swelling > 30 mm	65	18		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Any, Grade 3 and Related Solicited General Symptoms after Booster Vaccination

End point title	Number of Subjects With Any, Grade 3 and Related Solicited General Symptoms after Booster Vaccination

End point description:

Solicited general AEs = drowsiness, irritability, loss of appetite and fever (axillary >= 37.5 degrees Celsius). Any= Incidence of any symptom regardless of intensity grade or relationship to vaccination. Grade 3: drowsiness = prevented normal activity. irritability = crying that could not be comforted/ prevented normal activity. loss of appetite = not eating at all. Fever = temperature > 39.5°C Related = symptom assessed by the investigator as related to the vaccination. The DTPa Group, at the time of the booster immunization, include subjects with or without Prevenar vaccination administered before the booster dose.

End point type	Secondary

End point timeframe:

During the 8-day (Days 0-7) period following booster vaccination

End point values	10Pn Group	DTPa Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	228	120		
Units: Subjects				
Any drowsiness	69	30		
Grade 3 drowsiness	3	3		
Related drowsiness	19	7		
Fever >= 37.5°C	90	24		
Fever > 39.5°C	6	0		
Related fever	41	11		
Any irritability	90	35		
Grade 3 irritability	8	2		
Related irritability	36	10		
Any loss of appetite	48	17		
Grade 3 loss of appetite	4	1		
Related loss of appetite	12	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Unsolicited AEs after Primary Vaccination

End point title	Number of Subjects With Unsolicited AEs after Primary Vaccination

End point description:

An unsolicited adverse event is any adverse event (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:

Within the 31-day (Days 0-30) post-primary vaccination period, across doses

End point values	10Pn Group	DTPa Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	237	123		
Units: Subjects				
Any AE(s)	193	97		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Unsolicited AEs after Booster Vaccination

End point title	Number of Subjects With Unsolicited AEs after Booster Vaccination

End point description:

An unsolicited adverse event is any adverse event (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. The DTPa Group, at the time of the booster immunization, include subjects with or without Prevenar vaccination administered before the booster dose.

End point type	Secondary

End point timeframe:

Within the 31-day (Days 0-30) post booster vaccination period

End point values	10Pn Group	DTPa Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	228	120		
Units: Subjects				
Any AE(s)	132	66		

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

End point type	Secondary

End point timeframe:

From study start at Month 0 up to study end at Month 15-17

End point values	10Pn Group	DTPa Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	237	123		
Units: Subjects				
Any SAE(s)	28	19		

Statistical analyses

No statistical analyses for this end point

Secondary: Opsonophagocytic Titers Against Vaccine Pneumococcal Serotypes (booster immunization)

End point title	Opsonophagocytic Titers Against Vaccine Pneumococcal Serotypes (booster immunization)[14]

End point description:

Pneumococcal vaccine serotypes assessed were 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F and were calculated, expressed as GMTs. The seropositivity cut-off for the assay was >= 8. Antibody titers < 8 were given an arbitrary value of half the cut-off for the purpose of GMT calculation. Administration of catch-up pneumococcal vaccination with a licensed product other than Synflorix was allowed in the DTPa Group at least 7 days before DTPa vaccine booster dose. Thus, for this booster phase analysis, the DTPa Group was further split in DTPa + Prevenar Group and DTPa - no Prevenar Group. Lower and Upper Limits of the 95% confidence interval could not be calculated in the DTPa - no Prevenar Group because

number of subjects affected = 0: both limits have been entered = to GMC value (system constraint workaround).

End point type	Secondary

End point timeframe:

Prior to (PRE, at Month 14-16) and one month after booster (POST, at Month 15-17) immunization

Notes:

[14] - 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 participants from the 10Pn Group, the DTPa + Prevenar Group and the DTPa - no Prevenar Group.

End point values	10Pn Group	DTPa + Prevenar Group	DTPa - no Prevenar Group	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	214	113	1	
Units: Titer				
geometric mean (confidence interval 95%)				
OPSONO-1 PRE (N=214,113,1)	45.9 (34.9 to 60.4)	4.5 (4 to 5.1)	4 (-99999 to 99999)	
OPSONO-1 POST (N=214,112,1)	2320.7 (1941.8 to 2773.6)	4.7 (4.1 to 5.5)	4 (-99999 to 99999)	
OPSONO-4 PRE (N=205,105,1)	58.3 (43.6 to 77.9)	79 (49.3 to 126.7)	371 (-99999 to 99999)	
OPSONO-4 POST (N=214,109,1)	3863.1 (3319.7 to 4495.5)	69.3 (43.1 to 111.5)	493 (-99999 to 99999)	
OPSONO-5 PRE (N=212,113,1)	22.9 (19.1 to 27.6)	4.2 (3.9 to 4.5)	4 (-99999 to 99999)	
OPSONO-5 POST (N=214,112,1)	686.7 (583.8 to 807.9)	4.7 (4.1 to 5.3)	4 (-99999 to 99999)	
OPSONO-6B PRE (N=212,110,1)	191.2 (141.9 to 257.5)	118.5 (66.3 to 211.7)	4 (-99999 to 99999)	
OPSONO-6B POST (N=214,110,1)	1682.9 (1379.1 to 2053.7)	119 (68.5 to 206.9)	4 (-99999 to 99999)	
OPSONO-7F PRE (N=209,111,1)	2244.8 (1921.9 to 2621.9)	1014.7 (743.8 to 1384.1)	588 (-99999 to 99999)	
OPSONO-7F POST (N=214,112,1)	14144.3 (12109.3 to 16521.4)	1165.6 (855.7 to 1587.8)	1278 (-99999 to 99999)	
OPSONO-9V PRE (N=213,113,1)	520 (437.3 to 618.5)	1081.6 (803.3 to 1456.4)	4595 (-99999 to 99999)	
OPSONO-9V POST (N=214,112,1)	4693.7 (4099 to 5374.6)	958.8 (680 to 1351.8)	367 (-99999 to 99999)	
OPSONO-14 PRE (N=211,111,1)	673.1 (573.1 to 790.6)	826.7 (669.3 to 1021)	4 (-99999 to 99999)	
OPSONO-14 POST (N=213,112,1)	6209 (5299.3 to 7274.8)	819.1 (651.4 to 1030.1)	4 (-99999 to 99999)	
OPSONO-18C PRE (N=207,112,1)	26.3 (21.1 to 32.6)	11.5 (8.2 to 16)	4 (-99999 to 99999)	
OPSONO-18C POST (N=214,109,1)	2181 (1900.1 to 2503.4)	12.7 (9.1 to 17.7)	4 (-99999 to 99999)	
OPSONO-19F PRE (N=204,110,1)	83.4 (64.7 to 107.6)	21.1 (13.5 to 32.9)	4 (-99999 to 99999)	
OPSONO-19F POST (N=212,108,1)	3496.3 (2938.8 to 4159.6)	20.9 (13.7 to 31.8)	191 (-99999 to 99999)	

OPSONO-23F PRE (N=209,111,1)	600.5 (417.6 to 863.4)	1048 (561.5 to 1956.1)	4 (-99999 to 99999)	
OPSONO-23F POST (N=214,111,1)	7057.2 (5896.6 to 8446.1)	1758.3 (949.4 to 3256.5)	4 (-99999 to 99999)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited AEs: within 8 days (Day 0 - Day 7) after any vaccine dose; Unsolicited AEs: within 31 days (Day 0 - Day 30) after any vaccine dose.
SAEs: from Dose 1 up to Study End (Day 0 to Month 15-17).

Adverse event reporting additional description:

All-causes mortality, SAEs and other AEs data collection was analyzed for primary vaccination phase groups, including all vaccinated subjects in the study.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups

Reporting group title	10Pn Group

Reporting group description:

Healthy male or female subjects, between 90 and 118 days of age who received, during primary vaccination phase, 3 doses of Synflorix (10Pn) vaccine, administered intramuscularly on alternating (left/right) sides of the anterolateral thigh and DPT "KAKETSUKEN" Syringe (DTPa) vaccine administered subcutaneously on alternating (left/right) sides of the distal one third of the upper arm. Both vaccines were administered at 3, 4, and 5 months of age, followed by a booster dose at 17-19 months of age (booster vaccination phase).

Reporting group title	DTPa Group

Reporting group description:

Healthy male or female subjects, between 90 and 118 days of age, who received, during the primary vaccination phase, 3 doses of the DPT "KAKETSUKEN" Syringe (DTPa) vaccine, administered subcutaneously on alternating (left/right) sides of the distal one third of the upper arm at 3, 4, and 5 months of age, followed by a booster dose at 17-19 months of age (booster vaccination phase). Subjects from this group who also received at least one dose of Prevenar (PCV7): Pfizer's (formerly Wyeth Lederle) 7-valent pneumococcal conjugate vaccine, given before pre-booster blood sample (as optional treatment considered as standard of care), were assigned to the DTPa + Prevenar Group in the booster phase, and subjects who did not receive any dose of Prevenar before pre-booster blood sample were assigned to the DTPa-no Prevenar Group in the booster phase. Some booster phase analyses were only performed on subjects of both pooled DTPa sub-groups, at the time of the analysis.

Serious adverse events	10Pn Group	DTPa Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	28 / 237 (11.81%)	19 / 123 (15.45%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events			
Congenital, familial and genetic disorders			
Ear malformation			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 237 (0.42%)	0 / 123 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Faciodigitogenital dysplasia			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 237 (0.00%)	1 / 123 (0.81%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Kawasaki’s disease			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 237 (0.42%)	0 / 123 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Febrile convulsion			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 237 (0.84%)	0 / 123 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Convulsion			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 237 (0.42%)	0 / 123 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelitis transverse			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 237 (0.42%)	0 / 123 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 237 (0.42%)	0 / 123 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden infant death syndrome			

alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 237 (0.42%)	0 / 123 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Immune system disorders			
Food allergy			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 237 (0.00%)	1 / 123 (0.81%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Strabismus			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 237 (0.00%)	1 / 123 (0.81%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Intussusception			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 237 (0.00%)	1 / 123 (0.81%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal polyp			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 237 (0.42%)	0 / 123 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 237 (0.84%)	1 / 123 (0.81%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fibrinous bronchitis			

alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 237 (0.00%)	1 / 123 (0.81%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract inflammation			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 237 (0.42%)	0 / 123 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Tuberculid			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 237 (0.00%)	1 / 123 (0.81%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
alternative assessment type: Non-systematic			
subjects affected / exposed	6 / 237 (2.53%)	1 / 123 (0.81%)	
occurrences causally related to treatment / all	0 / 7	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	3 / 237 (1.27%)	3 / 123 (2.44%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	5 / 237 (2.11%)	1 / 123 (0.81%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Croup infectious			
alternative assessment type: Non-systematic			

subjects affected / exposed	0 / 237 (0.00%)	3 / 123 (2.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
alternative assessment type: Non-systematic			
subjects affected / exposed	3 / 237 (1.27%)	0 / 123 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis rotavirus			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 237 (0.84%)	1 / 123 (0.81%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopneumonia			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 237 (0.42%)	1 / 123 (0.81%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 237 (0.84%)	0 / 123 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngotonsillitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 237 (0.42%)	1 / 123 (0.81%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus bronchiolitis			
alternative assessment type: Non-systematic			

subjects affected / exposed	1 / 237 (0.42%)	1 / 123 (0.81%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 237 (0.84%)	0 / 123 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 237 (0.00%)	2 / 123 (1.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute tonsillitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 237 (0.00%)	1 / 123 (0.81%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Exanthema subitum			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 237 (0.42%)	0 / 123 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis norovirus			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 237 (0.00%)	1 / 123 (0.81%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 237 (0.00%)	1 / 123 (0.81%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Laryngitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 237 (0.00%)	1 / 123 (0.81%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis staphylococcal			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 237 (0.42%)	0 / 123 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 237 (0.42%)	0 / 123 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia adenoviral			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 237 (0.42%)	0 / 123 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia bacterial			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 237 (0.42%)	0 / 123 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia respiratory syncytial viral			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 237 (0.00%)	1 / 123 (0.81%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral pharyngitis			
alternative assessment type: Non-systematic			

subjects affected / exposed	0 / 237 (0.00%)	1 / 123 (0.81%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	10Pn Group	DTPa Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	236 / 237 (99.58%)	122 / 123 (99.19%)	
Nervous system disorders			
Somnolence			
subjects affected / exposed	131 / 237 (55.27%)	63 / 123 (51.22%)	
occurrences (all)	244	113	
General disorders and administration site conditions			
Pain			
subjects affected / exposed	167 / 237 (70.46%)	62 / 123 (50.41%)	
occurrences (all)	354	115	
Swelling			
subjects affected / exposed	214 / 237 (90.30%)	113 / 123 (91.87%)	
occurrences (all)	610	265	
Pyrexia			
subjects affected / exposed	156 / 237 (65.82%)	64 / 123 (52.03%)	
occurrences (all)	284	92	
Injection site induration			
alternative assessment type: Non-systematic			
subjects affected / exposed	56 / 237 (23.63%)	23 / 123 (18.70%)	
occurrences (all)	86	34	
Drowsiness			
subjects affected / exposed	131 / 237 (55.27%)	63 / 123 (51.22%)	
occurrences (all)	244	113	
Eye disorders			
Conjunctivitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	18 / 237 (7.59%)	9 / 123 (7.32%)	
occurrences (all)	22	13	
Gastrointestinal disorders			

Diarrhoea			
alternative assessment type: Non-systematic			
subjects affected / exposed	29 / 237 (12.24%)	14 / 123 (11.38%)	
occurrences (all)	32	14	
Respiratory, thoracic and mediastinal disorders			
Rhinorrhoea			
alternative assessment type: Non-systematic			
subjects affected / exposed	14 / 237 (5.91%)	4 / 123 (3.25%)	
occurrences (all)	16	4	
Upper respiratory tract inflammation			
alternative assessment type: Non-systematic			
subjects affected / exposed	19 / 237 (8.02%)	7 / 123 (5.69%)	
occurrences (all)	20	9	
Skin and subcutaneous tissue disorders			
Eczema			
alternative assessment type: Non-systematic			
subjects affected / exposed	49 / 237 (20.68%)	25 / 123 (20.33%)	
occurrences (all)	65	28	
Dermatitis diaper			
alternative assessment type: Non-systematic			
subjects affected / exposed	15 / 237 (6.33%)	9 / 123 (7.32%)	
occurrences (all)	19	9	
Erythema			
alternative assessment type: Non-systematic			
subjects affected / exposed	230 / 237 (97.05%)	114 / 123 (92.68%)	
occurrences (all)	768	368	
Psychiatric disorders			
Irritability			
subjects affected / exposed	177 / 237 (74.68%)	81 / 123 (65.85%)	
occurrences (all)	358	154	
Infections and infestations			
Upper respiratory tract infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	85 / 237 (35.86%)	43 / 123 (34.96%)	
occurrences (all)	131	69	
Nasopharyngitis			

alternative assessment type: Non-systematic			
subjects affected / exposed	41 / 237 (17.30%)	24 / 123 (19.51%)	
occurrences (all)	60	41	
Bronchitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	17 / 237 (7.17%)	15 / 123 (12.20%)	
occurrences (all)	21	18	
Gastroenteritis			
alternative assessment type: Non-systematic			
subjects affected / exposed	18 / 237 (7.59%)	5 / 123 (4.07%)	
occurrences (all)	19	5	
Impetigo			
alternative assessment type: Non-systematic			
subjects affected / exposed	5 / 237 (2.11%)	8 / 123 (6.50%)	
occurrences (all)	5	9	
Otitis media			
alternative assessment type: Non-systematic			
subjects affected / exposed	9 / 237 (3.80%)	7 / 123 (5.69%)	
occurrences (all)	10	7	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	91 / 237 (38.40%)	37 / 123 (30.08%)	
occurrences (all)	133	43	

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