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	v1
This version publication date	05 April 2016
First version publication date	29 July 2015

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 1901/2006 apply to this trial?	Yes

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 re-sponses of the 10-valent pneumococcal conjugate vaccine as observed in the pivotal non-inferiority study 10PN-PD-DIT-001 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: -

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:

Subjects received 3 doses of 10Pn and DTPa vaccines at 3, 4, and 5 months of age, followed by a booster dose at 17-19 months of age.

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:

Subjects received 3 doses of the DTPa vaccine at 3, 4, and 5 months of age, followed by a booster dose at 17-19 months of age.
In the primary vaccination study period, the control group received a 3-dose vaccination course with DTPa alone. Administration of catch-up pneumococcal vaccination with a licensed product other than 10Pn was allowed in that group though at least 7 days before DTPa vaccine booster dose. Thus for some booster phase analyses, the DTPa group was further split as follows:
-DTPa_Pr Group: subjects with at least one dose of Prevenar® (PCV7): Pfizer's (formerly Wyeth Lederle) 7-valent pneumococcal conjugate vaccine,given before pre-booster blood sample
-DTPa_w_Pr Group: subjects with no PCV7 vaccination before pre-booster blood sample

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:	
Subjects received 3 doses of 10Pn and DTPa vaccines at 3, 4, and 5 months of age, followed by a booster dose at 17-19 months of age.	
Reporting group title	DTPa Group
Reporting group description:	
Subjects received 3 doses of the DTPa vaccine at 3, 4, and 5 months of age, followed by a booster dose at 17-19 months of age. In the primary vaccination study period, the control group received a 3-dose vaccination course with DTPa alone. Administration of catch-up pneumococcal vaccination with a licensed product other than 10Pn was allowed in that group though at least 7 days before DTPa vaccine booster dose. Thus for some booster phase analyses, the DTPa group was further split as follows: -DTPa_Pr Group: subjects with at least one dose of Prevenar® (PCV7): Pfizer's (formerly Wyeth Lederle) 7-valent pneumococcal conjugate vaccine,given before pre-booster blood sample -DTPa_w_Pr Group: subjects with no PCV7 vaccination before pre-booster blood sample	

Reporting group values	10Pn Group	DTPa Group	Total
Number of subjects	237	123	360
Age categorical Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			0
Newborns (0-27 days)			0
Infants and toddlers (28 days-23 months)			0
Children (2-11 years)			0
Adolescents (12-17 years)			0
Adults (18-64 years)			0
From 65-84 years			0
85 years and over			0
Age continuous Units: weeks			
arithmetic mean	13.6	13.5	
standard deviation	± 1.02	± 1.1	-
Gender categorical Units: Subjects			
Female	120	64	184
Male	117	59	176

End points

End points reporting groups

Reporting group title	10Pn Group

Reporting group description:

Subjects received 3 doses of 10Pn and DTPa vaccines at 3, 4, and 5 months of age, followed by a booster dose at 17-19 months of age.

Reporting group title	DTPa Group

Reporting group description:

Subjects received 3 doses of the DTPa vaccine at 3, 4, and 5 months of age, followed by a booster dose at 17-19 months of age.
In the primary vaccination study period, the control group received a 3-dose vaccination course with DTPa alone. Administration of catch-up pneumococcal vaccination with a licensed product other than 10Pn was allowed in that group though at least 7 days before DTPa vaccine booster dose. Thus for some booster phase analyses, the DTPa group was further split as follows:
-DTPa_Pr Group: subjects with at least one dose of Prevenar® (PCV7): Pfizer's (formerly Wyeth Lederle) 7-valent pneumococcal conjugate vaccine,given before pre-booster blood sample
-DTPa_w_Pr Group: subjects with no PCV7 vaccination before pre-booster blood sample

Subject analysis set title	DTPa_Pr Group
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects from the DTPA Group with at least one dose of PCV7 given before pre-booster blood sample.

Subject analysis set title	DTPa_Without Pr Group
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects from the DTPA Group with no PCV7 vaccination given before pre-booster blood sample

Subject analysis set title	10Pn-001 Group
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Pooled 10Pn vaccine groups (10PN-PD-DIT-001 study): subjects received 3-dose primary vaccination course at 2-3-4 months of age of 10Pn (3 different lots)+ Infanrix hexa™ (except for the second dose in France which was co-administered with Infanrix-IPV/Hib™) vaccines. The number of subjects in this subject analysis set = 1107 subjects (360 being a placeholder value)

Primary: Anti-pneumococcal Vaccine Serotype Antibody Concentrations(10Pn-001 and 10Pn groups)

End point title	Anti-pneumococcal Vaccine Serotype Antibody Concentrations(10Pn-001 and 10Pn groups)[1]

End point description:

Antibodies assessed for this outcome measure were those against the vaccine pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F (ANTI-1, -4, -5, -6B, -7F, -9V, -14, -18C, -19F and -23F). The seropositivity cut-off of the assay was an antibody concentration ≥ 0.05 µg/mL.

End point type	Primary

End point timeframe:

1 month following primary immunization (post-Dose 3)

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: The analysis of the primary endpoint concerns the Pooled 10Pn vaccine groups (10PN-PD-DIT-001 study) and the 10Pn group of the study.

End point values	10Pn Group	10Pn-001 Group		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	231	1107		
Units: µg/mL				
number (not applicable)				
Anti-1 (N=231,1100)	6.52	1.05		
Anti-4 (N=231,1106)	6.54	1.45		
Anti-5 (N=231,1104)	6.54	1.7		
Anti-6B (N=231,1100)	1.71	0.33		
Anti-7F (N=231,1107)	6.11	1.72		
Anti-9V (N=231,1103)	5.42	1.32		
Anti-14 (N=231,1100)	10.03	2.9		
Anti-18C (N=231,1102)	16.59	1.66		
Anti-19F (N=229,1104)	17.39	1.84		
Anti-23F (N=231,1102)	2.17	0.53		

Statistical analyses

Statistical analysis title	10Pn-001 over 10Pn- Anti-1 GMC ratio

Statistical analysis description:

At one month after primary immunization (post-dose 3), ELISA Geometric Mean Concentration (GMC) ratios (10Pn-001 Group over 10Pn Group) were calculated for each of the 10 pneumococcal serotypes

Comparison groups	10Pn Group v 10Pn-001 Group
Number of subjects included in analysis	1338
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
Parameter estimate	GMC ratio
Point estimate	0.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.14
upper limit	0.18

Notes:

[2] - Comparability to the 10PN-PD-DIT-001 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 10Pn Group of study 10PN-PD-DIT-001 over GMCs from 10Pn Group of the current study) was below a limit of 2-fold for all 10 vaccine pneumococcal serotypes.

Statistical analysis title	10Pn-001 over 10Pn- Anti-4 GMC ratio

Statistical analysis description:

At one month after primary immunization (post-dose 3), ELISA Geometric Mean Concentration (GMC) ratios (10Pn-001 Group over 10Pn Group) were calculated for each of the 10 pneumococcal serotypes

Comparison groups	10Pn Group v 10Pn-001 Group

Number of subjects included in analysis	1338
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
Parameter estimate	GMC ratio
Point estimate	0.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.2
upper limit	0.25

Notes:

[3] - Comparability to the 10PN-PD-DIT-001 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 10Pn Group of study 10PN-PD-DIT-001 over GMCs from 10Pn Group of the current study) was below a limit of 2-fold for all 10 vaccine pneumococcal serotypes.

Statistical analysis title	10Pn-001 over 10Pn- Anti-5 GMC ratio

Statistical analysis description:

At one month after primary immunization (post-dose 3), ELISA Geometric Mean Concentration (GMC) ratios (10Pn-001 Group over 10Pn Group) were calculated for each of the 10 pneumococcal serotypes

Comparison groups	10Pn Group v 10Pn-001 Group
Number of subjects included in analysis	1338
Analysis specification	Pre-specified
Analysis type	non-inferiority[4]
Parameter estimate	GMC ratio
Point estimate	0.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.23
upper limit	0.29

Notes:

[4] - Comparability to the 10PN-PD-DIT-001 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 10Pn Group of study 10PN-PD-DIT-001 over GMCs from 10Pn Group of the current study) was below a limit of 2-fold for all 10 vaccine pneumococcal serotypes.

Statistical analysis title	10Pn-001 over 10Pn- Anti-6B GMC ratio

Statistical analysis description:

At one month after primary immunization (post-dose 3), ELISA Geometric Mean Concentration (GMC) ratios (10Pn-001 Group over 10Pn Group) were calculated for each of the 10 pneumococcal serotypes

Comparison groups	10Pn Group v 10Pn-001 Group
Number of subjects included in analysis	1338
Analysis specification	Pre-specified
Analysis type	non-inferiority[5]
Parameter estimate	GMC ratio
Point estimate	0.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.16
upper limit	0.23

Notes:

[5] - Comparability to the 10PN-PD-DIT-001 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 10Pn Group of study 10PN-PD-DIT-001 over GMCs from 10Pn Group of the current study) was below a limit of 2-fold for all 10 vaccine pneumococcal serotypes.

Statistical analysis title	10Pn-001 over 10Pn- Anti-7F GMC ratio

Statistical analysis description:

At one month after primary immunization (post-dose 3), ELISA Geometric Mean Concentration (GMC) ratios (10Pn-001 Group over 10Pn Group) were calculated for each of the 10 pneumococcal serotypes

Comparison groups	10Pn Group v 10Pn-001 Group
Number of subjects included in analysis	1338
Analysis specification	Pre-specified
Analysis type	non-inferiority[6]
Parameter estimate	GMC ratio
Point estimate	0.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.25
upper limit	0.31

Notes:

[6] - Comparability to the 10PN-PD-DIT-001 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 10Pn Group of study 10PN-PD-DIT-001 over GMCs from 10Pn Group of the current study) was below a limit of 2-fold for all 10 vaccine pneumococcal serotypes.

Statistical analysis title	10Pn-001 over 10Pn- Anti-9V GMC ratio

Statistical analysis description:

At one month after primary immunization (post-dose 3), ELISA Geometric Mean Concentration (GMC) ratios (10Pn-001 Group over 10Pn Group) were calculated for each of the 10 pneumococcal serotypes

Comparison groups	10Pn Group v 10Pn-001 Group
Number of subjects included in analysis	1338
Analysis specification	Pre-specified
Analysis type	non-inferiority[7]
Parameter estimate	GMC ratio
Point estimate	0.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.22
upper limit	0.27

Notes:

[7] - Comparability to the 10PN-PD-DIT-001 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 10Pn Group of study 10PN-PD-DIT-001 over GMCs from 10Pn Group of the current study) was below a limit of 2-fold for all 10 vaccine pneumococcal serotypes.

Statistical analysis title	10Pn-001 over 10Pn- Anti-14 GMC ratio

Statistical analysis description:

At one month after primary immunization (post-dose 3), ELISA Geometric Mean Concentration (GMC) ratios (10Pn-001 Group over 10Pn Group) were calculated for each of the 10 pneumococcal serotypes

Comparison groups	10Pn Group v 10Pn-001 Group

Number of subjects included in analysis	1338
Analysis specification	Pre-specified
Analysis type	non-inferiority[8]
Parameter estimate	GMC ratio
Point estimate	0.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.25
upper limit	0.33

Notes:

[8] - Comparability to the 10PN-PD-DIT-001 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 10Pn Group of study 10PN-PD-DIT-001 over GMCs from 10Pn Group of the current study) was below a limit of 2-fold for all 10 vaccine pneumococcal serotypes.

Statistical analysis title	10Pn-001 over 10Pn- Anti-18C GMC ratio

Statistical analysis description:

At one month after primary immunization (post-dose 3), ELISA Geometric Mean Concentration (GMC) ratios (10Pn-001 Group over 10Pn Group) were calculated for each of the 10 pneumococcal serotypes

Comparison groups	10Pn Group v 10Pn-001 Group
Number of subjects included in analysis	1338
Analysis specification	Pre-specified
Analysis type	non-inferiority[9]
Parameter estimate	GMC ratio
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.09
upper limit	0.12

Notes:

[9] - Comparability to the 10PN-PD-DIT-001 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 10Pn Group of study 10PN-PD-DIT-001 over GMCs from 10Pn Group of the current study) was below a limit of 2-fold for all 10 vaccine pneumococcal serotypes.

Statistical analysis title	10Pn-001 over 10Pn- Anti-19F GMC ratio

Statistical analysis description:

At one month after primary immunization (post-dose 3), ELISA Geometric Mean Concentration (GMC) ratios (10Pn-001 Group over 10Pn Group) were calculated for each of the 10 pneumococcal serotypes

Comparison groups	10Pn Group v 10Pn-001 Group
Number of subjects included in analysis	1338
Analysis specification	Pre-specified
Analysis type	non-inferiority[10]
Parameter estimate	GMC ratio
Point estimate	0.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.09
upper limit	0.12

Notes:

[10] - Comparability to the 10PN-PD-DIT-001 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 10Pn Group of study 10PN-PD-DIT-001 over GMCs from 10Pn Group of the current study) was below a limit of 2-fold for all 10 vaccine pneumococcal serotypes.

Statistical analysis title	10Pn-001 over 10Pn- Anti-23F GMC ratio

Statistical analysis description:

At one month after primary immunization (post-dose 3), ELISA Geometric Mean Concentration (GMC) ratios (10Pn-001 Group over 10Pn Group) were calculated for each of the 10 pneumococcal serotypes

Comparison groups	10Pn Group v 10Pn-001 Group
Number of subjects included in analysis	1338
Analysis specification	Pre-specified
Analysis type	non-inferiority[11]
Parameter estimate	GMC ratio
Point estimate	0.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.21
upper limit	0.29

Notes:

[11] - Comparability to the 10PN-PD-DIT-001 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 10Pn Group of study 10PN-PD-DIT-001 over GMCs from 10Pn Group of the current study) was below a limit of 2-fold for all 10 vaccine pneumococcal serotypes.

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

End point title	Concentrations of antibodies against Vaccine Pneumococcal Serotypes (primary immunization).[12]

End point description:

Antibodies assessed for this outcome measure were those against the vaccine pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F (ANTI-1, -4, -5, -6B, -7F, -9V, -14, -18C, -19F and -23F). Antibody concentrations were measured by 22F enzyme-linked immunosorbent assay (ELISA), expressed as geometric mean concentrations (GMCs), in micrograms per milliliter (µg/mL). The seropositivity cut-off of the assay was an antibody concentration ≥ 0.05 µg/mL. 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	Primary

End point timeframe:

1 month following primary immunization (Post-dose 3)

Notes:

[12] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	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-1 (N=231,119)	6.52 (5.85 to 7.26)	0.04 (0.03 to 0.04)		
Anti-4 (N=231,120)	6.54 (5.86 to 7.3)	0.03 (0.03 to 0.03)		

Anti-5 (N=231,119)	6.54 (5.94 to 7.21)	0.05 (0.04 to 0.06)		
Anti-6B (N=231,121)	1.71 (1.43 to 2.05)	0.03 (0.03 to 0.03)		
Anti-7F (N=231,120)	6.11 (5.5 to 6.78)	0.03 (0.03 to 0.04)		
Anti-9V (N=231,119)	5.42 (4.81 to 6.1)	0.03 (0.03 to 0.03)		
Anti-14 (N=231,120)	10.03 (8.8 to 11.43)	0.07 (0.06 to 0.09)		
Anti-18C (N=231,121)	16.59 (14.4 to 19.13)	0.04 (0.03 to 0.04)		
Anti-19F (N=229,118)	17.39 (15.53 to 19.48)	0.06 (0.05 to 0.07)		
Anti-23F (N=231,119)	2.17 (1.83 to 2.57)	0.04 (0.03 to 0.04)		

Statistical analyses

No statistical analyses for this end point

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

End point title	Concentrations of Antibodies Against Vaccine Pneumococcal Serotypes (booster immunization).[13]

End point description:

Antibodies assessed for this outcome measure were those against the vaccine pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F (ANTI-1, -4, -5, -6B, -7F, -9V, -14, -18C, -19F and -23F). Antibody concentrations were measured by 22F enzyme-linked immunosorbent assay (ELISA), expressed as geometric mean concentrations (GMCs), in micrograms per milliliter (µg/mL). The seropositivity cut-off of the assay was an antibody concentration ≥ 0.05 µg/mL. Antibody concentrations < 0.05 µg/mL were given an arbitrary value of half the cut-off for the purpose of GMC calculation. The lower limit (LL) and upper limit (UL) of the 95% confidence interval could not be determined in the DTPa_Without Pr Group (not applicable because number of subjects with the event = 0): LL and UL has been entered as equal to GMC in such cases (= only values acceptable by the System).

End point type	Secondary

End point timeframe:

prior to (PRE) and one month after booster (POST) 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: The analysis of the secondary endpoint concerns the 10Pn group and both DTPa_Pr and DTPa_Without Pr Group (DTpa Group splitted for the booster phase analysis (see also additional "subject analysis set" definitions)

End point values	10Pn Group	DTPa_Pr Group	DTPa_Without Pr 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 (0.03 to 0.03)	
Anti-1 POST (N=214,114,1)	7.81 (6.91 to 8.82)	0.04 (0.04 to 0.05)	0.24 (0.24 to 0.24)	

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

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 (Post-Dose 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 microgram per millilitre (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 (Post-Dose 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).[14]

End point description:

Concentrations were given in microgram per millilitre (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. The lower limit (LL) and upper limit (UL) of the 95% confidence interval could not be determined in the DTPa_Without Pr Group (not applicable because number of subjects with the event = 0): LL and UL has been entered as equal to GMC in such cases (= only values acceptable by the System).

End point type	Secondary

End point timeframe:

prior to (PRE) and one month after booster (POST) 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: The analysis of the secondary endpoint concerns the 10Pn group and both DTPa_Pr and DTPa_Without Pr Group (DTpa Group splitted for the booster phase analysis (see also additional "subject analysis set" definitions)

End point values	10Pn Group	DTPa_Pr Group	DTPa_Without Pr 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 (0.03 to 0.03)	
Anti-6A POST (N=214,114,1)	2.72 (2.24 to 3.3)	0.21 (0.16 to 0.27)	0.03 (0.03 to 0.03)	
Anti-19A PRE (N=214,114,1)	0.57 (0.45 to 0.71)	0.12 (0.09 to 0.16)	0.03 (0.03 to 0.03)	
Anti-19A POST (N=214,114,1)	5.16 (4.18 to 6.37)	0.15 (0.11 to 0.2)	0.03 (0.03 to 0.03)	

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 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 (Post-Dose 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)[15]

End point description:

Cross-reactive pneumococcal vaccine serotypes assessed were 6A and 19A 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. The lower limit (LL) and upper limit (UL) of the 95% confidence interval could not be determined in the DTPa_Without Pr Group (not applicable because number of subjects with the event = 0): LL and UL has been entered as equal to GMC in such cases (= only values acceptable by the System).

End point type	Secondary

End point timeframe:

prior to (PRE) and one month after booster (POST) immunization

Notes:

[15] - 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: The analysis of the secondary endpoint concerns the 10Pn group and both DTPa_Pr and DTPa_Without Pr Group (DTpa Group splitted for the booster phase analysis (see also additional "subject analysis set" definitions)

End point values	10Pn Group	DTPa_Pr Group	DTPa_Without Pr Group	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	213	119	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 (4 to 4)	
OPSONO-6A POST (N=212,107,1)	767.9 (593.1 to 994.1)	103.3 (60.4 to 176.6)	4 (4 to 4)	
OPSONO-19A PRE (N=213,111,1)	13.1 (10.1 to 16.9)	7.7 (5.5 to 10.6)	4 (4 to 4)	
OPSONO-19A POST (N=212,119,1)	431.4 (330.9 to 562.4)	8.6 (6 to 12.2)	4 (4 to 4)	

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 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 < 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 (Post-Dose 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 Antibodies against Protein D (PD) (booster immunization)

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

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 < 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:

prior to (PRE) and one month after booster (POST) 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 geometric mean concentrations 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 (Post-Dose3)

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 Antibodies Against Diphtheria Toxoid (DT) and Tetanus Toxoid (TT)(booster immunization).

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

End point description:

Concentrations of antibodies are presented as geometric mean concentrations 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:

prior to (PRE) and one month after booster (POST) immunization

End point values	10Pn Group	DTPa Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	214	113		
Units: IU/mL				
geometric mean (confidence interval 95%)				
Anti-DT PRE (N=211,112)	0.615 (0.556 to 0.679)	0.717 (0.618 to 0.833)		
Anti-DT POST (N=214,113)	15.977 (14.573 to 17.515)	10.814 (9.684 to 12.075)		
Anti-TT PRE (N=210,113)	2.043 (1.677 to 2.489)	1.352 (1.038 to 1.762)		
Anti-TT POST (N=214,113)	11.057 (9.949 to 12.287)	6.278 (5.334 to 7.389)		

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 geometric mean concentrations expressed as Enzyme-Linked Immuno-Sorbent Assay (ELISA) units per millilitre (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 (Post-Dose 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 Antibodies against pertussis (PT) and filamentous haemagglutinin (FHA)(booster immunization)

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

End point description:

Concentrations of antibodies are presented as geometric mean concentrations expressed as Enzyme-Linked Immuno-Sorbent Assay (ELISA) units per millilitre (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:

prior to (PRE) and one month after booster (POST) 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-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 Adverse Events (AEs).

End point title	Number of Subjects With Any and Grade 3 Solicited Local Adverse Events (AEs).

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 Adverse Events (AEs).

End point title	Number of Subjects with Any, Grade 3 and Related Solicited General Adverse Events (AEs).

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. irritability = crying that could not be comforted/ prevented normal activity. loss of appetite = not eating at all.. Fever = > 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 Adverse Events (AEs).

End point title	Number of Subjects With Any and Grade 3 Solicited Local Adverse Events (AEs).

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) period following booster vaccination with Synflorix vaccine

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 Adverse Events (AEs).

End point title	Number of Subjects With Any, Grade 3 and Related Solicited General Adverse Events (AEs).

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.

End point type	Secondary

End point timeframe:

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

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.

End point title	Number of Subjects With Unsolicited AEs.

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

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.

End point title	Number of Subjects With Unsolicited AEs.

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 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

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)[16]

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. The lower limit (LL) and upper limit (UL) of the 95% confidence interval could not be determined in the DTPa_Without Pr Group (not applicable because number of subjects with the event = 0): LL and UL has been entered as equal to GMT in such cases (= only values acceptable by the System)

End point type	Secondary

End point timeframe:

prior to (PRE) and one month after booster (POST) immunization

Notes:

[16] - 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: The analysis of the secondary endpoint concerns the 10Pn group and both DTPa_Pr and DTPa_Without Pr Group (DTpa Group splitted for the booster phase analysis (see also additional "subject analysis set" definitions)

End point values	10Pn Group	DTPa_Pr Group	DTPa_Without Pr 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 (4 to 4)	
OPSONO-1 POST (N=214,112,1)	2320.7 (1941.8 to 2773.6)	4.7 (4.1 to 5.5)	4 (4 to 4)	
OPSONO-4 PRE (N=205,105,1)	58.3 (43.6 to 77.9)	79 (49.3 to 126.7)	371 (371 to 371)	
OPSONO-4 POST (N=214,109,1)	3863.1 (3319.7 to 4495.5)	69.3 (43.1 to 111.5)	493 (493 to 493)	
OPSONO-5 PRE (N=212,113,1)	22.9 (19.1 to 27.6)	4.2 (3.9 to 4.5)	4 (4 to 4)	
OPSONO-5 POST (N=214,112,1)	686.7 (583.8 to 807.9)	4.7 (4.1 to 5.3)	4 (4 to 4)	
OPSONO-6B PRE (N=212,110,1)	191.2 (141.9 to 257.5)	118.5 (66.3 to 211.7)	4 (4 to 4)	
OPSONO-6B POST (N=214,110,1)	1682.9 (1379.1 to 2053.7)	119 (68.5 to 206.9)	4 (4 to 4)	
OPSONO-7F PRE (N=209,111,1)	2244.8 (1921.9 to 2621.9)	1014.7 (743.8 to 1384.1)	588 (588 to 588)	
OPSONO-7F POST (N=214,112,1)	14144.3 (12109.3 to 16521.4)	1165.6 (855.7 to 1587.8)	1278 (1278 to 1278)	
OPSONO-9V PRE (N=213,113,1)	520 (437.3 to 618.5)	1081.6 (803.3 to 1456.4)	4595 (4595 to 4595)	
OPSONO-9V POST (N=214,112,1)	4693.7 (4099 to 5374.6)	958.8 (680 to 1351.8)	367 (367 to 367)	
OPSONO-14 PRE (N=211,111,1)	673.1 (573.1 to 790.6)	826.7 (669.3 to 1021)	4 (4 to 4)	
OPSONO-14 POST (N=213,112,1)	6209 (5299.3 to 7274.8)	819.1 (651.4 to 1030.1)	4 (4 to 4)	
OPSONO-18C PRE (N=207,112,1)	26.3 (21.1 to 32.6)	11.5 (8.2 to 16)	4 (4 to 4)	
OPSONO-18C POST (N=214,109,1)	2181 (1900.1 to 2503.4)	12.7 (9.1 to 17.7)	4 (4 to 4)	
OPSONO-19F PRE (N=204,110,1)	83.4 (64.7 to 107.6)	21.1 (13.5 to 32.9)	4 (4 to 4)	
OPSONO-19F POST (N=212,108,1)	3496.3 (2938.8 to 4159.6)	20.9 (13.7 to 31.8)	191 (191 to 191)	
OPSONO-23F PRE (N=209,111,1)	600.5 (417.6 to 863.4)	1048 (561.5 to 1956.1)	4 (4 to 4)	
OPSONO-23F POST (N=214,111,1)	7057.2 (5896.6 to 8446.1)	1758.3 (949.4 to 3256.5)	4 (4 to 4)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

SAEs: from Month 0 up to study end. Unsolicited AEs: within the 31-day post-primary and post booster vaccination period. Solicited AEs: During the 8-day period following the primary and booster vaccination.

Adverse event reporting additional description:

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

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	15.0

Reporting groups

Reporting group title	10Pn Group

Reporting group description:

Subjects received 3 doses of 10Pn and DTPa vaccines at 3, 4, and 5 months of age, followed by a booster dose at 17-19 months of age.

Reporting group title	DTPa Group

Reporting group description:

Subjects received 3 doses of the DTPa vaccine at 3, 4, and 5 months of age, followed by a booster dose at 17-19 months of age.
In the primary vaccination study period, the control group received a 3-dose vaccination course with DTPa alone. Administration of catch-up pneumococcal vaccination with a licensed product other than 10Pn was allowed in that group though at least 7 days before DTPa vaccine booster dose. Thus for some booster phase analyses, the DTPa group was further split as follows:
-DTPa_Pr Group: subjects with at least one dose of Prevenar® (PCV7): Pfizer's (formerly Wyeth Lederle) 7-valent pneumococcal conjugate vaccine,given before pre-booster blood sample
-DTPa_w_Pr Group: subjects with no PCV7 vaccination before pre-booster blood sample

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			
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			
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			
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			
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			
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	
Myelitis transverse			
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			
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			
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			
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			

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			
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			
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			
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			
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			
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			
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			

subjects affected / exposed	6 / 237 (2.53%)	1 / 123 (0.81%)	
occurrences causally related to treatment / all	0 / 6	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	3 / 237 (1.27%)	3 / 123 (2.44%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus infection			
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			
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			
subjects affected / exposed	3 / 237 (1.27%)	0 / 123 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis rotavirus			
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			
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			
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			

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			
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			
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			
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			
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			
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			
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			
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			

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	
Meningitis staphylococcal			
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			
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			
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			
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			
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			
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	221 / 237 (93.25%)	107 / 123 (86.99%)	
General disorders and administration site conditions			
Pain (Primary epoch)			
alternative assessment type: Systematic			
subjects affected / exposed	120 / 237 (50.63%)	42 / 123 (34.15%)	
occurrences (all)	120	42	
Redness (Primary epoch)			
alternative assessment type: Systematic			
subjects affected / exposed	221 / 237 (93.25%)	107 / 123 (86.99%)	
occurrences (all)	221	107	
Swelling (Primary epoch)			
alternative assessment type: Systematic			
subjects affected / exposed	188 / 237 (79.32%)	90 / 123 (73.17%)	
occurrences (all)	188	90	
Pain (Booster epoch)			
alternative assessment type: Systematic			
subjects affected / exposed[1]	134 / 228 (58.77%)	47 / 120 (39.17%)	
occurrences (all)	134	47	
Redness (Booster epoch)			
alternative assessment type: Systematic			
subjects affected / exposed[2]	197 / 228 (86.40%)	102 / 120 (85.00%)	
occurrences (all)	197	102	
Swelling (Booster epoch)			
alternative assessment type: Systematic			
subjects affected / exposed[3]	180 / 228 (78.95%)	90 / 120 (75.00%)	
occurrences (all)	180	90	
Drowsiness (Primary epoch)			
alternative assessment type: Systematic			
subjects affected / exposed	110 / 237 (46.41%)	50 / 123 (40.65%)	
occurrences (all)	110	50	
Fever (Axillary) (Primary epoch)			
alternative assessment type: Systematic			

subjects affected / exposed	110 / 237 (46.41%)	49 / 123 (39.84%)	
occurrences (all)	110	49	
Irritability (Primary epoch)			
alternative assessment type: Systematic			
subjects affected / exposed	152 / 237 (64.14%)	70 / 123 (56.91%)	
occurrences (all)	152	70	
Loss of appetite (Primary epoch)			
alternative assessment type: Systematic			
subjects affected / exposed	61 / 237 (25.74%)	24 / 123 (19.51%)	
occurrences (all)	61	24	
Drowsiness (Booster epoch)			
alternative assessment type: Systematic			
subjects affected / exposed[4]	69 / 228 (30.26%)	30 / 120 (25.00%)	
occurrences (all)	69	30	
Fever (Axillary) (Booster epoch)			
alternative assessment type: Systematic			
subjects affected / exposed[5]	90 / 228 (39.47%)	24 / 120 (20.00%)	
occurrences (all)	90	24	
Irritability (Booster epoch)			
alternative assessment type: Systematic			
subjects affected / exposed[6]	90 / 228 (39.47%)	35 / 120 (29.17%)	
occurrences (all)	90	35	
Loss of appetite (Booster epoch)			
alternative assessment type: Systematic			
subjects affected / exposed[7]	48 / 228 (21.05%)	17 / 120 (14.17%)	
occurrences (all)	48	17	
Injection site induration (Primary epoch)			
subjects affected / exposed	39 / 237 (16.46%)	18 / 123 (14.63%)	
occurrences (all)	39	18	
Injection site induration (Booster epoch)			
subjects affected / exposed[8]	28 / 228 (12.28%)	9 / 120 (7.50%)	
occurrences (all)	28	9	
Eye disorders			

Conjunctivitis			
subjects affected / exposed	14 / 237 (5.91%)	7 / 123 (5.69%)	
occurrences (all)	14	7	
Gastrointestinal disorders			
Diarrhoea (Primary epoch)			
subjects affected / exposed	23 / 237 (9.70%)	8 / 123 (6.50%)	
occurrences (all)	23	8	
Diarrhoea (Booster epoch)			
subjects affected / exposed[9]	7 / 228 (3.07%)	6 / 120 (5.00%)	
occurrences (all)	7	6	
Respiratory, thoracic and mediastinal disorders			
Rhinorrhoea			
subjects affected / exposed	12 / 237 (5.06%)	2 / 123 (1.63%)	
occurrences (all)	12	2	
Upper respiratory tract inflammation			
subjects affected / exposed[10]	13 / 228 (5.70%)	5 / 120 (4.17%)	
occurrences (all)	13	5	
Skin and subcutaneous tissue disorders			
Eczema (Primary epoch)			
subjects affected / exposed	45 / 237 (18.99%)	20 / 123 (16.26%)	
occurrences (all)	45	20	
Dermatitis diaper			
subjects affected / exposed	15 / 237 (6.33%)	8 / 123 (6.50%)	
occurrences (all)	15	8	
Erythema			
subjects affected / exposed	10 / 237 (4.22%)	11 / 123 (8.94%)	
occurrences (all)	10	11	
Eczema (Booster epoch)			
subjects affected / exposed[11]	6 / 228 (2.63%)	7 / 120 (5.83%)	
occurrences (all)	6	7	
Infections and infestations			
Upper respiratory tract infection (Primary epoch)			
subjects affected / exposed	64 / 237 (27.00%)	33 / 123 (26.83%)	
occurrences (all)	64	33	
Nasopharyngitis (Primary epoch)			

subjects affected / exposed	32 / 237 (13.50%)	17 / 123 (13.82%)	
occurrences (all)	32	17	
Bronchitis (Primary epoch)			
subjects affected / exposed	12 / 237 (5.06%)	7 / 123 (5.69%)	
occurrences (all)	12	7	
Gastroenteritis			
subjects affected / exposed	15 / 237 (6.33%)	3 / 123 (2.44%)	
occurrences (all)	15	3	
Impetigo			
subjects affected / exposed	3 / 237 (1.27%)	7 / 123 (5.69%)	
occurrences (all)	3	7	
Upper respiratory tract infection (Booster epoch)			
subjects affected / exposed[12]	34 / 228 (14.91%)	17 / 120 (14.17%)	
occurrences (all)	34	17	
Nasopharyngitis (Booster epoch)			
subjects affected / exposed[13]	15 / 228 (6.58%)	11 / 120 (9.17%)	
occurrences (all)	15	11	
Bronchitis (Booster epoch)			
subjects affected / exposed[14]	5 / 228 (2.19%)	9 / 120 (7.50%)	
occurrences (all)	5	9	
Hand-foot-and-mouth disease			
subjects affected / exposed[15]	5 / 228 (2.19%)	6 / 120 (5.00%)	
occurrences (all)	5	6	

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Adverse Event results are presented only for subjects for whom results were available.

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Adverse Event results are presented only for subjects for whom results were available.

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Adverse Event results are presented only for subjects for whom results were available.

[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Adverse Event results are presented only for subjects for whom results were available.

[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Adverse Event results are presented only for subjects for whom results were available.

[6] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Adverse Event results are presented only for subjects for whom results were available.

[7] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Adverse Event results are presented only for subjects for whom results were available.

[8] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Adverse Event results are presented only for subjects for whom results were available.

[9] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Adverse Event results are presented only for subjects for whom results were available.

[10] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Adverse Event results are presented only for subjects for whom results were available.

[11] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Adverse Event results are presented only for subjects for whom results were available.

[12] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Adverse Event results are presented only for subjects for whom results were available.

[13] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Adverse Event results are presented only for subjects for whom results were available.

[14] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Adverse Event results are presented only for subjects for whom results were available.

[15] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Adverse Event results are presented only for subjects for whom results were available.

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