Clinical trial results:
A Phase 3, Randomized, Double-Blind Trial to Evaluate the Safety and Immunogenicity of a 20-valent Pneumococcal Conjugate Vaccine in Healthy Infants

Summary

EudraCT number	2019-003305-10
Trial protocol	Outside EU/EEA
Global end of trial date	02 September 2022

Results information

Result version number	v1 (current)
This version publication date	15 March 2023
First version publication date	15 March 2023

Trial information

Trial identification

Sponsor protocol code	B7471011

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04382326
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, NY 10017
Public contact	Pfizer Inc., Pfizer ClinicalTrials.gov Call Center, 001 18007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer Inc., Pfizer ClinicalTrials.gov Call Center, 001 18007181021, ClinicalTrials.gov_Inquiries@pfizer.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	07 October 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	02 September 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Safety: To describe the safety profile of 20vPnC. Safety assessments included local reactions, systemic events and adverse events.
Immunogenicity: Noninferiority of IgG GMCs (2-fold criterion) at 1 month after Dose 4 (co-primary) and 1 month after Dose 3 (key secondary); Percentage of participants with predefined IgG concentrations 1 month after Dose 3 (co-primary; 10% Noninferiority criterion); Noninferiority of percentage of participants with prespecified antibody levels to specific concomitant vaccine antigens 1 month after Dose 3. The 7 additional serotypes in the 20vPnC group were compared with the lowest result among vaccine serotypes in the 13vPnC group for noninferiority evaluation of pneumococcal endpoints.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Council for Harmonisation (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 May 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 1774
Country: Number of subjects enrolled	Puerto Rico: 214
Worldwide total number of subjects	1988
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)	1988
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:

A total of 1997 subjects were enrolled and randomized in the study. Six subjects did not receive any study vaccine. Three subjects who received incorrect study vaccine during the study were excluded.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	20vPnC

Arm description:

Infants 42 to 98 days of age were enrolled to receive 4 doses of 0.5 millilitre (mL) 20-valent Pneumococcal Conjugate Vaccine (20vPnC) intramuscularly. Dose 1 was given at enrollment and Dose 2 and 3 were given 42 to 63 days from the previous dose. Dose 4 was administered at 365 to 455 days of age.

Arm type	Experimental
Investigational medicinal product name	20-valent pneumococcal conjugate vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received a single dose (0.5 mL) of 20vPnC intramuscularly into the anterolateral thigh muscle of the left leg at each vaccination visit (Doses 1, 2, 3, and 4 at Visits 1, 2, 3, and 5, respectively).

Arm title	13vPnC

Arm description:

Infants 42 to 98 days of age were enrolled to receive 4 doses of 0.5 millilitre (mL) 13-valent Pneumococcal Conjugate Vaccine (13vPnC) intramuscularly. Dose 1 was given at enrollment and Dose 2 and 3 were given 42 to 63 days from the previous dose. Dose 4 was administered at 365 to 455 days of age.

Arm type	Active comparator
Investigational medicinal product name	13-valent pneumococcal conjugate vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received a single dose (0.5 mL) of 13vPnC intramuscularly into the anterolateral thigh muscle of the left leg at each vaccination visit (Doses 1, 2, 3, and 4 at Visits 1, 2, 3, and 5, respectively).

Number of subjects in period 1	20vPnC	13vPnC
Started	1001	987
Completed	821	799
Not completed	180	188
Physician decision	-	1
Adverse Event, not serious	1	2
Withdrawal By Parent/Guardian	50	54
Adverse event, non-fatal	1	1
Unspecified	1	-
No Longer Meets Eligibility Criteria	50	44
Lost to follow-up	48	63
Protocol deviation	29	23

Baseline characteristics

Reporting groups	
Reporting group title	20vPnC
Reporting group description:	
Infants 42 to 98 days of age were enrolled to receive 4 doses of 0.5 millilitre (mL) 20-valent Pneumococcal Conjugate Vaccine (20vPnC) intramuscularly. Dose 1 was given at enrollment and Dose 2 and 3 were given 42 to 63 days from the previous dose. Dose 4 was administered at 365 to 455 days of age.	
Reporting group title	13vPnC
Reporting group description:	
Infants 42 to 98 days of age were enrolled to receive 4 doses of 0.5 millilitre (mL) 13-valent Pneumococcal Conjugate Vaccine (13vPnC) intramuscularly. Dose 1 was given at enrollment and Dose 2 and 3 were given 42 to 63 days from the previous dose. Dose 4 was administered at 365 to 455 days of age.	

Reporting group values	20vPnC	13vPnC	Total
Number of subjects	1001	987	1988
Age Categorical Units: Participants			
Infants and Toddlers(28 days - 23 months) Days	1001	987	1988
Age Continuous Units: Days			
arithmetic mean	65.9	65.6	
standard deviation	± 7.98	± 7.12	-
Sex: Female, Male Units: Participants			
Female	483	482	965
Male	518	505	1023
Race/Ethnicity, Customized Units: Subjects			
White	754	742	1496
Black or African American	110	108	218
Asian	16	16	32
American Indian or Alaska Native	4	3	7
Native Hawaiian or other Pacific Islander	2	2	4
Multiracial	68	73	141
Not reported	47	43	90
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic/Latino	312	293	605
Non-Hispanic/non-Latino	661	659	1320
Not reported	28	35	63
Age Range Units: Days			
median	64.0	64.0	
full range (min-max)	42 to 97	43 to 96	-

End points

End points reporting groups

Reporting group title	20vPnC

Reporting group description:

Infants 42 to 98 days of age were enrolled to receive 4 doses of 0.5 millilitre (mL) 20-valent Pneumococcal Conjugate Vaccine (20vPnC) intramuscularly. Dose 1 was given at enrollment and Dose 2 and 3 were given 42 to 63 days from the previous dose. Dose 4 was administered at 365 to 455 days of age.

Reporting group title	13vPnC

Reporting group description:

Infants 42 to 98 days of age were enrolled to receive 4 doses of 0.5 millilitre (mL) 13-valent Pneumococcal Conjugate Vaccine (13vPnC) intramuscularly. Dose 1 was given at enrollment and Dose 2 and 3 were given 42 to 63 days from the previous dose. Dose 4 was administered at 365 to 455 days of age.

Primary: Percentage of Subjects With Local Reactions Within 7 Days After Dose 1

End point title	Percentage of Subjects With Local Reactions Within 7 Days After Dose 1[1]

End point description:

Local reactions were recorded using an electronic diary. Local reactions included redness, swelling and pain at the injection site. Redness and swelling were graded as mild (0.5 to 2.0 cm), moderate (>2.0 to 7.0 cm) and severe (>7.0 cm). Pain at injection site was graded as mild (hurt if gently touched example, whimpered, winced, protested, or withdrew), moderate (hurt if gently touched, with crying), and severe (caused limitation of limb movement). Safety population included all the subjects who received at least 1 dose of the investigational product (IP) with safety follow up after any dose. Here, 'Number of Subjects Analyzed' = number of subjects with any electronic diary (e-diary) data reported after Dose 1.

End point type	Primary

End point timeframe:

Within 7 days after Dose 1

Notes:

[1] - 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: Only descriptive data was planned to be analyzed for this endpoint.

End point values	20vPnC	13vPnC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	993	974		
Units: Percentage of subjects				
number (confidence interval 95%)				
Redness: Any	25.5 (22.8 to 28.3)	24.6 (22.0 to 27.5)		
Redness: Mild	21.5 (18.9 to 24.1)	22.3 (19.7 to 25.0)		
Redness: Moderate	4.0 (2.9 to 5.4)	2.4 (1.5 to 3.5)		
Redness: Severe	0 (0.0 to 0.4)	0 (0.0 to 0.4)		
Swelling: Any	16.4 (14.2 to 18.9)	18.8 (16.4 to 21.4)		
Swelling: Mild	11.5 (9.6 to 13.6)	14.7 (12.5 to 17.1)		
Swelling: Moderate	4.8 (3.6 to 6.4)	4.1 (2.9 to 5.6)		
Swelling: Severe	0.1 (0.0 to 0.6)	0 (0.0 to 0.4)		

Pain at the injection site: Any	49.1 (46.0 to 52.3)	45.3 (42.1 to 48.5)		
Pain at the injection site: Mild	30.6 (27.8 to 33.6)	30.4 (27.5 to 33.4)		
Pain at the injection site: Moderate	18.4 (16.1 to 21.0)	14.9 (12.7 to 17.3)		
Pain at the injection site: Severe	0.1 (0.0 to 0.6)	0 (0.0 to 0.4)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Local Reactions Within 7 Days After Dose 2

End point title	Percentage of Subjects With Local Reactions Within 7 Days After Dose 2[2]

End point description:

Local reactions were recorded using an electronic diary. Local reactions included redness, swelling and pain at the injection site. Redness and swelling were graded as mild (0.5 to 2.0 cm), moderate (>2.0 to 7.0 cm) and severe (>7.0 cm). Pain at injection site was graded as mild (hurt if gently touched example, whimpered, winced, protested, or withdrew), moderate (hurt if gently touched, with crying), and severe (caused limitation of limb movement). Safety population included all the subjects who received at least 1 dose of the investigational product (IP) with safety follow up after any dose. Here, 'Number of Subjects Analyzed' = number of subjects with any electronic diary (e-diary) data reported after Dose 2.

End point type	Primary

End point timeframe:

Within 7 Days After Dose 2

Notes:

[2] - 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: Only descriptive data was planned to be analyzed for this endpoint.

End point values	20vPnC	13vPnC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	940	924		
Units: Percentage of subjects				
number (confidence interval 95%)				
Redness: Any	23.2 (20.5 to 26.0)	26.4 (23.6 to 29.4)		
Redness: Mild	21.2 (18.6 to 23.9)	23.1 (20.4 to 25.9)		
Redness: Moderate	2.0 (1.2 to 3.1)	3.4 (2.3 to 4.7)		
Redness: Severe	0 (0.0 to 0.4)	0 (0.0 to 0.4)		
Swelling: Any	15.5 (13.3 to 18.0)	17.3 (14.9 to 19.9)		
Swelling: Mild	11.5 (9.5 to 13.7)	13.5 (11.4 to 15.9)		
Swelling: Moderate	4.0 (2.9 to 5.5)	3.8 (2.7 to 5.2)		
Swelling: Severe	0 (0.0 to 0.4)	0 (0.0 to 0.4)		
Pain at the injection site: Any	44.0 (40.8 to 47.3)	41.7 (38.5 to 44.9)		
Pain at the injection site: Mild	29.3 (26.4 to 32.3)	27.7 (24.8 to 30.7)		
Pain at the injection site: Moderate	14.8 (12.6 to 17.2)	14.0 (11.8 to 16.4)		

Pain at the injection site: Severe	0 (0.0 to 0.4)	0 (0.0 to 0.4)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Local Reactions Within 7 Days After Dose 3

End point title	Percentage of Subjects With Local Reactions Within 7 Days After Dose 3[3]

End point description:

Local reactions were recorded using an electronic diary. Local reactions included redness, swelling and pain at the injection site. Redness and swelling were graded as mild (0.5 to 2.0 cm), moderate (>2.0 to 7.0 cm) and severe (>7.0 cm). Pain at injection site was graded as mild (hurt if gently touched example, whimpered, winced, protested, or withdrew), moderate (hurt if gently touched, with crying), and severe (caused limitation of limb movement). Safety population included all the subjects who received at least 1 dose of the investigational product (IP) with safety follow up after any dose. Here, 'Number of Subjects Analyzed' = number of subjects with any electronic diary (e-diary) data reported after Dose 3.

End point type	Primary

End point timeframe:

Within 7 days after Dose 3

Notes:

[3] - 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: Only descriptive data was planned to be analyzed for this endpoint.

End point values	20vPnC	13vPnC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	914	901		
Units: Percentage of subjects				
number (confidence interval 95%)				
Redness: Any	25.4 (22.6 to 28.3)	27.2 (24.3 to 30.2)		
Redness: Mild	21.1 (18.5 to 23.9)	23.5 (20.8 to 26.4)		
Redness: Moderate	4.3 (3.1 to 5.8)	3.7 (2.5 to 5.1)		
Redness: Severe	0 (0.0 to 0.4)	0 (0.0 to 0.4)		
Swelling: Any	17.1 (14.7 to 19.7)	17.6 (15.2 to 20.3)		
Swelling: Mild	12.5 (10.4 to 14.8)	13.8 (11.6 to 16.2)		
Swelling: Moderate	4.6 (3.3 to 6.2)	3.8 (2.6 to 5.2)		
Swelling: Severe	0 (0.0 to 0.4)	0.1 (0.0 to 0.6)		
Pain at the injection site: Any	38.6 (35.5 to 41.9)	39.0 (35.8 to 42.2)		
Pain at the injection site: Mild	25.7 (22.9 to 28.7)	25.5 (22.7 to 28.5)		
Pain at the injection site: Moderate	12.9 (10.8 to 15.3)	13.4 (11.3 to 15.8)		
Pain at the injection site: Severe	0 (0.0 to 0.4)	0 (0.0 to 0.4)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Local Reactions Within 7 Days After Dose 4

End point title	Percentage of Subjects With Local Reactions Within 7 Days After Dose 4[4]

End point description:

Local reactions were recorded using an electronic diary. Local reactions included redness, swelling and pain at the injection site. Redness and swelling were graded as mild (0.5 to 2.0 cm), moderate (>2.0 to 7.0 cm) and severe (>7.0 cm). Pain at injection site was graded as mild (hurt if gently touched example, whimpered, winced, protested, or withdrew), moderate (hurt if gently touched, with crying), and severe (caused limitation of limb movement). Safety population included all the subjects who received at least 1 dose of the investigational product (IP) with safety follow up after any dose. Here, 'Number of Subjects Analyzed' = number of subjects with any electronic diary (e-diary) data reported after Dose 4.

End point type	Primary

End point timeframe:

Within 7 days after Dose 4

Notes:

[4] - 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: Only descriptive data was planned to be analyzed for this endpoint.

End point values	20vPnC	13vPnC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	826	815		
Units: Percentage of subjects				
number (confidence interval 95%)				
Redness: Any	23.5 (20.6 to 26.5)	26.6 (23.6 to 29.8)		
Redness: Mild	19.6 (17.0 to 22.5)	22.0 (19.2 to 25.0)		
Redness: Moderate	3.9 (2.7 to 5.4)	4.7 (3.3 to 6.3)		
Redness: Severe	0 (0.0 to 0.4)	0 (0.0 to 0.5)		
Swelling: Any	14.9 (12.5 to 17.5)	17.3 (14.8 to 20.1)		
Swelling: Mild	10.7 (8.6 to 13.0)	13.6 (11.3 to 16.2)		
Swelling: Moderate	4.2 (3.0 to 5.8)	3.7 (2.5 to 5.2)		
Swelling: Severe	0 (0.0 to 0.4)	0 (0.0 to 0.5)		
Pain at the injection site: Any	35.7 (32.4 to 39.1)	35.8 (32.5 to 39.2)		
Pain at the injection site: Mild	24.1 (21.2 to 27.2)	27.1 (24.1 to 30.3)		
Pain at the injection site: Moderate	11.3 (9.2 to 13.6)	8.7 (6.9 to 10.9)		
Pain at the injection site: Severe	0.4 (0.1 to 1.1)	0 (0.0 to 0.5)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Systemic Events Within 7 Days After Dose 1

End point title	Percentage of Subjects With Systemic Events Within 7 Days After Dose 1[5]

End point description:

Systemic events included fever, decreased appetite, drowsiness/increased sleep, and irritability. Fever was defined as an axillary temperature greater than or equal to (>=)38.0 degrees Celsius (C); decreased appetite was graded as mild (decreased interest in eating), moderate (decreased oral intake) and severe (refusal to feed); drowsiness was graded as mild (increased or prolonged sleeping bouts), moderate (slightly subdued, interfered with daily activity) and severe (disabling, not interested in usual daily activity); irritability: graded as mild (easily consolable), moderate (required increased attention) and severe (inconsolable, crying could not be comforted). Safety population included all the subjects who received at least 1 dose of the IP with safety follow up after any dose. 'Number of Subjects Analyzed' = number of subjects with any e-diary data reported after Dose 1.

End point type	Primary

End point timeframe:

Within 7 days after Dose 1

Notes:

[5] - 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: Only descriptive data was planned to be analyzed for this endpoint.

End point values	20vPnC	13vPnC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	993	974		
Units: Percentage of subjects				
number (confidence interval 95%)				
Fever: >=38.0 degree C	10.3 (8.5 to 12.3)	7.5 (5.9 to 9.3)		
Fever: >=38.0 degree C to 38.4 degree C	7.3 (5.7 to 9.0)	6.3 (4.8 to 8.0)		
Fever: >38.4 degree C to 38.9 degree C	2.2 (1.4 to 3.3)	0.9 (0.4 to 1.7)		
Fever: >38.9 degree C to 40.0 degree C	0.7 (0.3 to 1.4)	0.3 (0.1 to 0.9)		
Fever: >40.0 degree C	0.1 (0.0 to 0.6)	0 (0.0 to 0.4)		
Decreased appetite: Any	24.4 (21.7 to 27.2)	23.9 (21.3 to 26.7)		
Decreased appetite: Mild	14.5 (12.4 to 16.8)	16.1 (13.9 to 18.6)		
Decreased appetite: Moderate	9.7 (7.9 to 11.7)	7.5 (5.9 to 9.3)		
Decreased appetite: Severe	0.2 (0.0 to 0.7)	0.3 (0.1 to 0.9)		
Drowsiness: Any	67.2 (64.2 to 70.1)	66.0 (62.9 to 69.0)		
Drowsiness: Mild	50.2 (47.0 to 53.3)	49.3 (46.1 to 52.5)		
Drowsiness: Moderate	16.1 (13.9 to 18.5)	15.6 (13.4 to 18.0)		

Drowsiness: Severe	0.9 (0.4 to 1.7)	1.1 (0.6 to 2.0)		
Irritability: Any	70.9 (68.0 to 73.7)	71.7 (68.7 to 74.5)		
Irritability: Mild	23.4 (20.8 to 26.1)	21.6 (19.0 to 24.3)		
Irritability: Moderate	43.0 (39.9 to 46.1)	46.2 (43.0 to 49.4)		
Irritability: Severe	4.5 (3.3 to 6.0)	3.9 (2.8 to 5.3)		
Use of antipyretic or pain medication	35.1 (32.2 to 38.2)	33.8 (30.8 to 36.8)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Systemic Events Within 7 Days After Dose 2

End point title	Percentage of Subjects With Systemic Events Within 7 Days After Dose 2[6]

End point description:

Systemic events included fever, decreased appetite, drowsiness/increased sleep, and irritability. Fever was defined as an axillary temperature greater than or equal to (>=)38.0 degrees C; decreased appetite was graded as mild (decreased interest in eating), moderate (decreased oral intake) and severe (refusal to feed); drowsiness was graded as mild (increased or prolonged sleeping bouts), moderate (slightly subdued, interfered with daily activity) and severe (disabling, not interested in usual daily activity); irritability: graded as mild (easily consolable), moderate (required increased attention) and severe (inconsolable, crying could not be comforted). Safety population included all the subjects who received at least 1 dose of the IP with safety follow up after any dose. 'Number of Subjects Analyzed' = number of subjects with any e-diary data reported after Dose 2.

End point type	Primary

End point timeframe:

Within 7 days after Dose 2

Notes:

[6] - 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: Only descriptive data was planned to be analyzed for this endpoint.

End point values	20vPnC	13vPnC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	940	924		
Units: Percentage of subjects				
number (confidence interval 95%)				
Fever: >=38.0 degree C	17.3 (15.0 to 19.9)	16.3 (14.0 to 18.9)		
Fever: >=38.0 degree C to 38.4 degree C	10.9 (8.9 to 13.0)	10.0 (8.1 to 12.1)		
Fever: >38.4 degree C to 38.9 degree C	4.0 (2.9 to 5.5)	4.2 (3.0 to 5.7)		
Fever: >38.9 degree C to 40.0 degree C	2.2 (1.4 to 3.4)	2.2 (1.3 to 3.3)		
Fever: >40.0 degree C	0.2 (0.0 to 0.8)	0 (0.0 to 0.4)		
Decreased appetite: Any	26.4 (23.6 to 29.3)	23.5 (20.8 to 26.4)		
Decreased appetite: Mild	16.4 (14.1 to 18.9)	15.3 (13.0 to 17.7)		
Decreased appetite: Moderate	9.8 (8.0 to 11.9)	7.7 (6.0 to 9.6)		
Decreased appetite: Severe	0.2 (0.0 to 0.8)	0.5 (0.2 to 1.3)		

Drowsiness: Any	54.7 (51.4 to 57.9)	55.6 (52.4 to 58.9)		
Drowsiness: Mild	37.0 (33.9 to 40.2)	36.9 (33.8 to 40.1)		
Drowsiness: Moderate	16.9 (14.6 to 19.5)	17.9 (15.4 to 20.5)		
Drowsiness: Severe	0.7 (0.3 to 1.5)	0.9 (0.4 to 1.7)		
Irritability: Any	71.6 (68.6 to 74.5)	68.8 (65.7 to 71.8)		
Irritability: Mild	22.9 (20.2 to 25.7)	21.2 (18.6 to 24.0)		
Irritability: Moderate	44.7 (41.5 to 47.9)	43.4 (40.2 to 46.7)		
Irritability: Severe	4.0 (2.9 to 5.5)	4.2 (3.0 to 5.7)		
Use of antipyretic or pain medication	40.7 (37.6 to 44.0)	41.0 (37.8 to 44.3)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Systemic Events Within 7 Days After Dose 3

End point title	Percentage of Subjects With Systemic Events Within 7 Days After Dose 3[7]

End point description:

Systemic events included fever, decreased appetite, drowsiness/increased sleep, and irritability. Fever was defined as an axillary temperature greater than or equal to (>=)38.0 degrees C; decreased appetite was graded as mild (decreased interest in eating), moderate (decreased oral intake) and severe (refusal to feed); drowsiness was graded as mild (increased or prolonged sleeping bouts), moderate (slightly subdued, interfered with daily activity) and severe (disabling, not interested in usual daily activity); irritability: graded as mild (easily consolable), moderate (required increased attention) and severe (inconsolable, crying could not be comforted). Safety population included all the subjects who received at least 1 dose of the IP with safety follow up after any dose. 'Number of Subjects Analyzed' = number of subjects with any e-diary data reported after Dose 3.

End point type	Primary

End point timeframe:

Within 7 days after Dose 3

Notes:

[7] - 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: Only descriptive data was planned to be analyzed for this endpoint.

End point values	20vPnC	13vPnC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	914	901		
Units: Percentage of subjects				
number (confidence interval 95%)				
Fever: >=38.0 degree C	12.6 (10.5 to 14.9)	13.7 (11.5 to 16.1)		
Fever: >=38.0 degree C to 38.4 degree C	7.7 (6.0 to 9.6)	7.9 (6.2 to 9.8)		
Fever: >38.4 degree C to 38.9 degree C	3.4 (2.3 to 4.8)	3.9 (2.7 to 5.4)		
Fever: >38.9 degree C to 40.0 degree C	1.4 (0.8 to 2.4)	1.9 (1.1 to 3.0)		
Fever: >40.0 degree C	0.1 (0.0 to 0.6)	0 (0.0 to 0.4)		

Decreased appetite: Any	20.6 (18.0 to 23.3)	22.4 (19.7 to 25.3)		
Decreased appetite: Mild	13.5 (11.3 to 15.8)	13.9 (11.7 to 16.3)		
Decreased appetite: Moderate	6.7 (5.1 to 8.5)	8.2 (6.5 to 10.2)		
Decreased appetite: Severe	0.4 (0.1 to 1.1)	0.3 (0.1 to 1.0)		
Drowsiness: Any	44.1 (40.8 to 47.4)	44.1 (40.8 to 47.4)		
Drowsiness: Mild	31.1 (28.1 to 34.2)	30.1 (27.1 to 33.2)		
Drowsiness: Moderate	12.5 (10.4 to 14.8)	13.1 (11.0 to 15.5)		
Drowsiness: Severe	0.5 (0.2 to 1.3)	0.9 (0.4 to 1.7)		
Irritability: Any	64.4 (61.2 to 67.5)	63.0 (59.8 to 66.2)		
Irritability: Mild	25.2 (22.4 to 28.1)	21.6 (19.0 to 24.5)		
Irritability: Moderate	37.5 (34.4 to 40.8)	39.2 (36.0 to 42.5)		
Irritability: Severe	1.8 (1.0 to 2.8)	2.2 (1.4 to 3.4)		
Use of antipyretic/pain medication	36.3 (33.2 to 39.5)	36.1 (32.9 to 39.3)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Systemic Events Within 7 Days After Dose 4

End point title	Percentage of Subjects With Systemic Events Within 7 Days After Dose 4[8]

End point description:

Systemic events included fever, decreased appetite, drowsiness/increased sleep, and irritability. Fever was defined as an axillary temperature greater than or equal to (>=)38.0 degrees Celsius (C); decreased appetite was graded as mild (decreased interest in eating), moderate (decreased oral intake) and severe (refusal to feed); drowsiness was graded as mild (increased or prolonged sleeping bouts), moderate (slightly subdued, interfered with daily activity) and severe (disabling, not interested in usual daily activity); Irritability: graded as mild (easily consolable), moderate (required increased attention) and severe (inconsolable, crying could not be comforted). Safety population included all the subjects who received at least 1 dose of the IP with safety follow up after any dose. 'Number of Subjects Analyzed' = number of subjects with any e-diary data reported after Dose 4.

End point type	Primary

End point timeframe:

Within 7 days after Dose 4

Notes:

[8] - 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: Only descriptive data was planned to be analyzed for this endpoint.

End point values	20vPnC	13vPnC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	826	815		
Units: Percentage of subjects				
number (confidence interval 95%)				

Fever: >= 38.0 degree C	14.5 (12.2 to 17.1)	14.0 (11.7 to 16.6)		
Fever: >=38.0 degree C to 38.4 degree C	6.5 (4.9 to 8.4)	7.7 (6.0 to 9.8)		
Fever: >38.4 degree C to 38.9 degree C	5.1 (3.7 to 6.8)	3.2 (2.1 to 4.6)		
Fever: >38.9 degree C to 40.0 degree C	2.7 (1.7 to 4.0)	2.9 (1.9 to 4.4)		
Fever: >40.0 degree C	0.2 (0.0 to 0.9)	0.1 (0.0 to 0.7)		
Decreased appetite: Any	24.8 (21.9 to 27.9)	25.2 (22.2 to 28.3)		
Decreased appetite: Mild	15.9 (13.4 to 18.5)	16.1 (13.6 to 18.8)		
Decreased appetite: Moderate	8.6 (6.8 to 10.7)	8.3 (6.5 to 10.5)		
Decreased appetite: Severe	0.4 (0.1 to 1.1)	0.7 (0.3 to 1.6)		
Drowsiness: Any	39.5 (36.1 to 42.9)	39.5 (36.1 to 43.0)		
Drowsiness: Mild	27.8 (24.8 to 31.0)	28.2 (25.2 to 31.4)		
Drowsiness: Moderate	11.0 (9.0 to 13.4)	10.7 (8.6 to 13.0)		
Drowsiness: Severe	0.6 (0.2 to 1.4)	0.6 (0.2 to 1.4)		
Irritability: Any	61.0 (57.6 to 64.4)	61.1 (57.7 to 64.5)		
Irritability: Mild	23.4 (20.5 to 26.4)	21.8 (19.0 to 24.8)		
Irritability: Moderate	35.0 (31.7 to 38.3)	37.9 (34.6 to 41.3)		
Irritability: Severe	2.7 (1.7 to 4.0)	1.3 (0.7 to 2.4)		
Use of antipyretic/pain medication	37.5 (34.2 to 40.9)	36.7 (33.4 to 40.1)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Adverse Events (AEs) From Dose 1 to 1 Month After Dose 3

End point title	Percentage of Subjects With Adverse Events (AEs) From Dose 1 to 1 Month After Dose 3[9]

End point description:

An AE was any untoward medical occurrence in a subject, temporally associated with the use of study treatment, whether or not considered related to the study treatment. Safety population included all the subjects who received at least 1 dose of the IP with safety follow up after any dose. Here, 'Number of Subjects Analyzed' = number of subjects who received Dose 1.

End point type	Primary

End point timeframe:

From Dose 1 to 1 Month after Dose 3

Notes:

[9] - 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: Only descriptive data was planned to be analyzed for this endpoint.

End point values	20vPnC	13vPnC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1001	987		
Units: Percentage of subjects				
number (confidence interval 95%)	36.6 (33.6 to 39.6)	39.4 (36.3 to 42.5)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With AEs from Dose 4 to 1 Month After Dose 4

End point title	Percentage of Subjects With AEs from Dose 4 to 1 Month After Dose 4[10]

End point description:

An AE was any untoward medical occurrence in a subject, temporally associated with the use of study treatment, whether or not considered related to the study treatment. Safety population included all the subjects who received at least 1 dose of the IP with safety follow up after any dose. Here, 'Number of Subjects Analyzed' = number of subjects who received Dose 4 and had safety follow up after Dose 4.

End point type	Primary

End point timeframe:

From Dose 4 to 1 month after Dose 4

Notes:

[10] - 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: Only descriptive data was planned to be analyzed for this endpoint.

End point values	20vPnC	13vPnC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	853	841		
Units: Percentage of subjects				
number (confidence interval 95%)	15.1 (12.8 to 17.7)	15.0 (12.6 to 17.6)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Serious Adverse Events (SAEs) From Dose 1 to 6 Months Following Dose 4

End point title	Percentage of Subjects With Serious Adverse Events (SAEs) From Dose 1 to 6 Months Following Dose 4[11]

End point description:

A SAE was any untoward medical occurrence that, at any dose: resulted in death; required inpatient hospitalisation or prolongation of existing hospitalisation; was life-threatening; resulted in persistent or significant disability/ incapacity; congenital anomaly/birth defect and other important medical events. Safety population included all the subjects who received at least 1 dose of the IP with safety follow up after any dose. Here, 'Number of Subjects Analyzed' = number of subjects who received Dose 1.

End point type	Primary

End point timeframe:

From Dose 1 to 6 months following Dose 4

Notes:

[11] - 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: Only descriptive data was planned to be analyzed for this endpoint.

End point values	20vPnC	13vPnC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1001	987		
Units: Percentage of subjects				
number (confidence interval 95%)	4.5 (3.3 to 6.0)	3.1 (2.1 to 4.4)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Newly Diagnosed Chronic Medical Conditions (NDCMCs) From Dose 1 to 6 Months Following Dose 4

End point title	Percentage of Subjects With Newly Diagnosed Chronic Medical Conditions (NDCMCs) From Dose 1 to 6 Months Following Dose 4[12]

End point description:

An NDCMC was defined as a significant disease or medical condition, not previously identified, that was expected to be persistent or was otherwise long-lasting in its effects. Safety population included all the subjects who received at least 1 dose of the IP with safety follow up after any dose. Here, 'Number of Subjects Analyzed' = number of subjects who received Dose 1.

End point type	Primary

End point timeframe:

From Dose 1 to 6 months following Dose 4

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: Only descriptive data was planned to be analyzed for this endpoint.

End point values	20vPnC	13vPnC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1001	987		
Units: Percentage of subjects				
number (confidence interval 95%)	5.0 (3.7 to 6.5)	5.9 (4.5 to 7.5)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Predefined Serotype-specific Immunoglobulin G (IgG) Concentrations 1 Month After Dose 3

End point title	Percentage of Subjects With Predefined Serotype-specific Immunoglobulin G (IgG) Concentrations 1 Month After Dose 3

End point description:

Pre-specified levels of serotypes were as follows: for serotype 1, 3, 4, 6A, 7F, 9V, 14, 18C, 19F, 23F, 8, 10A, 11A, 12F, 15B, 22F, 33F: >=0.35 microgram per mL (mcg/mL), for serotype 5: >=0.23 mcg/mL, for serotype 6B: >=0.10 mcg/mL and for serotype 19A: >=0.12 mcg/mL. "Numbers of Subjects Analyzed" were the denominators and numbers of participants with an IgG concentration ≥ the predefined level for the given serotype were the numerator for the percentage calculations. 95% CI was based on the Clopper and Pearson method. Dose 3 evaluable population: eligible subjects aged 42-98 days on Dose 1, received the first 3 doses to which they were randomized, have at least 1 valid immunogenicity result within 27 to 56 days post Dose 3, and had no other major protocol deviations as determined by the clinician. Here, "Number of Subjects Analyzed" = number of participants with valid IgG concentrations for the specified serotype reported at 1 month after Dose 3.

End point type	Primary

End point timeframe:

1 month after Dose 3

End point values	20vPnC	13vPnC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	833	803		
Units: percentage of subjects				
number (confidence interval 95%)				
Serotype 1 (n=833, 802)	79.8 (76.9 to 82.5)	88.4 (86.0 to 90.5)		
Serotype 3 (n=833, 802)	52.1 (48.6 to 55.5)	67.6 (64.2 to 70.8)		
Serotype 4 (n=833, 802)	79.7 (76.8 to 82.4)	88.2 (85.7 to 90.3)		
Serotype 5 (n=833, 802)	82.5 (79.7 to 85.0)	86.8 (84.2 to 89.1)		
Serotype 6A (n=833, 802)	93.5 (91.6 to 95.1)	95.9 (94.3 to 97.2)		
Serotype 6B (n=831, 801)	88.3 (85.9 to 90.4)	92.4 (90.3 to 94.1)		
Serotype 7F (n=833, 802)	96.6 (95.2 to 97.8)	97.6 (96.3 to 98.6)		
Serotype 9V (n=833, 802)	81.9 (79.1 to 84.4)	89.8 (87.5 to 91.8)		
Serotype 14 (n=832, 802)	93.4 (91.5 to 95.0)	94.1 (92.3 to 95.7)		
Serotype 18C (n=833, 802)	92.6 (90.6 to 94.2)	93.1 (91.2 to 94.8)		
Serotype 19A (n=833, 802)	97.1 (95.7 to 98.1)	98.1 (96.9 to 98.9)		
Serotype 19F (n=833, 802)	96.9 (95.5 to 98.0)	96.6 (95.1 to 97.8)		
Serotype 23F (n=833, 802)	77.9 (74.9 to 80.7)	85.5 (82.9 to 87.9)		
Serotype 8 (n=833, 794)	96.8 (95.3 to 97.9)	1.6 (0.9 to 2.8)		
Serotype 10A (n=833, 803)	82.2 (79.5 to 84.8)	1.2 (0.6 to 2.3)		
Serotype 11A (n=833, 803)	92.7 (90.7 to 94.4)	1.5 (0.8 to 2.6)		
Serotype 12F (n=833, 803)	67.5 (64.2 to 70.6)	0.1 (0.0 to 0.7)		
Serotype 15B (n=833, 803)	98.2 (97.0 to 99.0)	2.6 (1.6 to 4.0)		

Serotype 22F (n=833, 803)	98.3 (97.2 to 99.1)	0.9 (0.4 to 1.8)		
Serotype 33F (n=833, 802)	86.7 (84.2 to 88.9)	1.1 (0.5 to 2.1)		

Statistical analyses

Statistical analysis title	NI of 20vPnC-13vPnC for matched serotype

Statistical analysis description:

Serotype 1: 2-Sided CI were calculated based on the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage

Comparison groups	20vPnC v 13vPnC
Number of subjects included in analysis	1636
Analysis specification	Pre-specified
Analysis type	non-inferiority[13]
Parameter estimate	percentage difference
Point estimate	-8.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.1
upper limit	-5.1

Notes:

[13] - Comparison was conducted for the 13 matched serotypes for 20vPnC to the corresponding serotype in 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the percentage differences (20vPnC - 13vPnC) was greater than -10%.

Statistical analysis title	NI of 20vPnC-13vPnC for 13 matched serotype

Statistical analysis description:

Serotype 4: 2-Sided CI were calculated based on the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage

Comparison groups	20vPnC v 13vPnC
Number of subjects included in analysis	1636
Analysis specification	Pre-specified
Analysis type	non-inferiority[14]
Parameter estimate	percentage difference
Point estimate	-8.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12
upper limit	-4.9

Notes:

[14] - Comparison was conducted for the 13 matched serotypes for 20vPnC to the corresponding serotype in 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the percentage differences (20vPnC - 13vPnC) was greater than -10%.

Statistical analysis title	NI of 20vPnC-13vPnC for 13 matched serotype

Statistical analysis description:

Serotype 3: 2-Sided CI were calculated based on the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage

Comparison groups	20vPnC v 13vPnC

Number of subjects included in analysis	1636
Analysis specification	Pre-specified
Analysis type	non-inferiority[15]
Parameter estimate	percentage difference
Point estimate	-15.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-20.1
upper limit	-10.8

Notes:

[15] - Comparison was conducted for the 13 matched serotypes for 20vPnC to the corresponding serotype in 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the percentage differences (20vPnC - 13vPnC) was greater than -10%.

Statistical analysis title	NI of 20vPnC-13vPnC for 13 matched serotype

Statistical analysis description:

Serotype 5: 2-Sided CI were calculated based on the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage

Comparison groups	20vPnC v 13vPnC
Number of subjects included in analysis	1636
Analysis specification	Pre-specified
Analysis type	non-inferiority[16]
Parameter estimate	percentage difference
Point estimate	-4.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.8
upper limit	-0.8

Notes:

[16] - Comparison was conducted for the 13 matched serotypes for 20vPnC to the corresponding serotype in 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the percentage differences (20vPnC - 13vPnC) was greater than -10%.

Statistical analysis title	NI of 20vPnC-13vPnC for 13 matched serotype

Statistical analysis description:

Serotype 6A: 2-Sided CI were calculated based on the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage

Comparison groups	20vPnC v 13vPnC
Number of subjects included in analysis	1636
Analysis specification	Pre-specified
Analysis type	non-inferiority[17]
Parameter estimate	percentage difference
Point estimate	-2.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.6
upper limit	-0.2

Notes:

[17] - Comparison was conducted for the 13 matched serotypes for 20vPnC to the corresponding serotype in 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the percentage differences (20vPnC - 13vPnC) was greater than -10%.

Statistical analysis title	NI of 20vPnC-13vPnC for 13 matched serotype

Statistical analysis description:

Serotype 6B: 2-Sided CI were calculated based on the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage

Comparison groups	20vPnC v 13vPnC
Number of subjects included in analysis	1636
Analysis specification	Pre-specified
Analysis type	non-inferiority[18]
Parameter estimate	percentage difference
Point estimate	-4.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7
upper limit	-1.2

Notes:

[18] - Comparison was conducted for the 13 matched serotypes for 20vPnC to the corresponding serotype in 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the percentage differences (20vPnC - 13vPnC) was greater than -10%.

Statistical analysis title	NI of 20vPnC-13vPnC for 13 matched serotype

Statistical analysis description:

Serotype 14: 2-Sided CI were calculated based on the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage

Comparison groups	20vPnC v 13vPnC
Number of subjects included in analysis	1636
Analysis specification	Pre-specified
Analysis type	non-inferiority[19]
Parameter estimate	percentage difference
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.1
upper limit	1.6

Notes:

[19] - Comparison was conducted for the 13 matched serotypes for 20vPnC to the corresponding serotype in 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the percentage differences (20vPnC - 13vPnC) was greater than -10%.

Statistical analysis title	NI of 20vPnC-13vPnC for 13 matched serotype

Statistical analysis description:

Serotype 9V: 2-Sided CI were calculated based on the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage

Comparison groups	20vPnC v 13vPnC
Number of subjects included in analysis	1636
Analysis specification	Pre-specified
Analysis type	non-inferiority[20]
Parameter estimate	percentage difference
Point estimate	-7.9

Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.3
upper limit	-4.6

Notes:

[20] - Comparison was conducted for the 13 matched serotypes for 20vPnC to the corresponding serotype in 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the percentage differences (20vPnC - 13vPnC) was greater than -10%.

Statistical analysis title	NI of 20vPnC-13vPnC for 13 matched serotype

Statistical analysis description:

Serotype 7F: 2-sided CI were calculated based on the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage

Comparison groups	20vPnC v 13vPnC
Number of subjects included in analysis	1636
Analysis specification	Pre-specified
Analysis type	non-inferiority[21]
Parameter estimate	percentage difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.7
upper limit	0.7

Notes:

[21] - Comparison was conducted for the 13 matched serotypes for 20vPnC to the corresponding serotype in 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the percentage differences (20vPnC - 13vPnC) was greater than -10%.

Statistical analysis title	NI of 20vPnC-13vPnC for 13 matched serotype

Statistical analysis description:

Serotype 18C: 2-Sided CI were calculated based on the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage

Comparison groups	20vPnC v 13vPnC
Number of subjects included in analysis	1636
Analysis specification	Pre-specified
Analysis type	non-inferiority[22]
Parameter estimate	percentage difference
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.1
upper limit	1.9

Notes:

[22] - Comparison was conducted for the 13 matched serotypes for 20vPnC to the corresponding serotype in 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the percentage differences (20vPnC - 13vPnC) was greater than -10%.

Statistical analysis title	NI of 20vPnC-13vPnC for 13 matched serotype

Statistical analysis description:

Serotype 19F: 2-Sided CI were calculated based on the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage

Comparison groups	20vPnC v 13vPnC

Number of subjects included in analysis	1636
Analysis specification	Pre-specified
Analysis type	non-inferiority[23]
Parameter estimate	percentage difference
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	2

Notes:

[23] - Comparison was conducted for the 13 matched serotypes for 20vPnC to the corresponding serotype in 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the percentage differences (20vPnC - 13vPnC) was greater than -10%.

Statistical analysis title	NI of 20vPnC-13vPnC for 13 matched serotype

Statistical analysis description:

Serotype 19A: 2-Sided CI were calculated based on the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage

Comparison groups	20vPnC v 13vPnC
Number of subjects included in analysis	1636
Analysis specification	Pre-specified
Analysis type	non-inferiority[24]
Parameter estimate	percentage difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.6
upper limit	0.5

Notes:

[24] - Comparison was conducted for the 13 matched serotypes for 20vPnC to the corresponding serotype in 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the percentage differences (20vPnC - 13vPnC) was greater than -10%.

Statistical analysis title	NI of 20vPnC-13vPnC for 13 matched serotype

Statistical analysis description:

Serotype 23F: 2-Sided CI were calculated based on the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage

Comparison groups	20vPnC v 13vPnC
Number of subjects included in analysis	1636
Analysis specification	Pre-specified
Analysis type	non-inferiority[25]
Parameter estimate	percentage difference
Point estimate	-7.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.4
upper limit	-3.9

Notes:

[25] - Comparison was conducted for the 13 matched serotypes for 20vPnC to the corresponding serotype in 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the percentage differences (20vPnC - 13vPnC) was greater than -10%.

Statistical analysis title	NI of 20vPnC - 13vPnC for 7 additional serotype

Statistical analysis description:

Serotype 8: 2-Sided CI were calculated based on the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage

Comparison groups	20vPnC v 13vPnC
Number of subjects included in analysis	1636
Analysis specification	Pre-specified
Analysis type	non-inferiority[26]
Parameter estimate	percentage difference
Point estimate	11.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	8.6
upper limit	14

Notes:

[26] - For the additional 7 serotypes, the compared results were from serotype 23F (13vPnC serotype with the lowest percentage, not including serotype 3) in the 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the percentage differences (20vPnC - lowest 13vPnC) was greater than -10%.

Statistical analysis title	NI of 20vPnC - 13vPnC for 7 additional serotype

Statistical analysis description:

Serotype 10A: 2-Sided CI were calculated based on the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage

Comparison groups	20vPnC v 13vPnC
Number of subjects included in analysis	1636
Analysis specification	Pre-specified
Analysis type	other[27]
Parameter estimate	percentage difference
Point estimate	-3.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.9
upper limit	0.3

Notes:

[27] - For the additional 7 serotypes, the compared results were from serotype 23F (13vPnC serotype with the lowest percentage, not including serotype 3) in the 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the percentage differences (20vPnC - lowest 13vPnC) was greater than -10%.

Statistical analysis title	NI of 20vPnC - 13vPnC for 7 additional serotype

Statistical analysis description:

Serotype 11A: 2-Sided CI were calculated based on the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage

Comparison groups	20vPnC v 13vPnC
Number of subjects included in analysis	1636
Analysis specification	Pre-specified
Analysis type	non-inferiority[28]
Parameter estimate	percentage difference
Point estimate	7.1

Confidence interval	
level	95 %
sides	2-sided
lower limit	4.2
upper limit	10.2

Notes:

[28] - For the additional 7 serotypes, the compared results were from serotype 23F (13vPnC serotype with the lowest percentage, not including serotype 3) in the 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the percentage differences (20vPnC - lowest 13vPnC) was greater than -10%.

Statistical analysis title	NI of 20vPnC - 13vPnC for 7 additional serotype

Statistical analysis description:

Serotype 12F: 2-Sided CI were calculated based on the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage

Comparison groups	20vPnC v 13vPnC
Number of subjects included in analysis	1636
Analysis specification	Pre-specified
Analysis type	non-inferiority[29]
Parameter estimate	percentage difference
Point estimate	-18.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-22.1
upper limit	-14

Notes:

[29] - For the additional 7 serotypes, the compared results were from serotype 23F (13vPnC serotype with the lowest percentage, not including serotype 3) in the 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the percentage differences (20vPnC - lowest 13vPnC) was greater than -10%.

Statistical analysis title	NI of 20vPnC - 13vPnC for 7 additional serotype

Statistical analysis description:

Serotype 22F: 2-Sided CI were calculated based on the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage

Comparison groups	20vPnC v 13vPnC
Number of subjects included in analysis	1636
Analysis specification	Pre-specified
Analysis type	non-inferiority[30]
Parameter estimate	percentage difference
Point estimate	12.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	10.3
upper limit	15.5

Notes:

[30] - For the additional 7 serotypes, the compared results were from serotype 23F (13vPnC serotype with the lowest percentage, not including serotype 3) in the 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the percentage differences (20vPnC - lowest 13vPnC) was greater than -10%.

Statistical analysis title	NI of 20vPnC - 13vPnC for 7 additional serotype

Statistical analysis description:

Serotype 15B: 2-Sided CI were calculated based on the Miettinen and Nurminen method for the

difference in proportions, expressed as a percentage

Comparison groups	20vPnC v 13vPnC
Number of subjects included in analysis	1636
Analysis specification	Pre-specified
Analysis type	non-inferiority[31]
Parameter estimate	percentage difference
Point estimate	12.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	10.2
upper limit	15.4

Notes:

[31] - For the additional 7 serotypes, the compared results were from serotype 23F (13vPnC serotype with the lowest percentage, not including serotype 3) in the 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the percentage differences (20vPnC - lowest 13vPnC) was greater than -10%.

Statistical analysis title	NI of 20vPnC - 13vPnC for 7 additional serotype

Statistical analysis description:

Serotype 33F: 2-Sided CI were calculated based on the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage

Comparison groups	20vPnC v 13vPnC
Number of subjects included in analysis	1636
Analysis specification	Pre-specified
Analysis type	non-inferiority[32]
Parameter estimate	percentage difference
Point estimate	1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.2
upper limit	4.5

Notes:

[32] - For the additional 7 serotypes, the compared results were from serotype 23F (13vPnC serotype with the lowest percentage, not including serotype 3) in the 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the percentage differences (20vPnC - lowest 13vPnC) was greater than -10%.

Primary: Serotype-specific IgG Geometric Mean Concentrations (GMCs) and Geometric Mean Ratios (GMRs) at 1 Month After Dose 4

End point title	Serotype-specific IgG Geometric Mean Concentrations (GMCs) and Geometric Mean Ratios (GMRs) at 1 Month After Dose 4

End point description:

Concentrations of anticapsular IgG for the 20 pneumococcal serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F, 8, 10A, 11A, 12F, 15B, 22F, and 33F) were determined in all subjects at 1 month after Dose 4 using the Luminex assay. Results were expressed as IgG concentrations. GMCs and 2-sided CIs were calculated by exponentiating the mean logarithm of the concentrations and the corresponding CIs based on the Student's t distribution. Dose 4 evaluable immunogenicity population: eligible subjects aged 42-98 days on Dose 1, received all 4 doses to which they were randomized, and were 365 to 455 days of age, inclusive, on the day of Dose 4, had at least 1 valid immunogenicity result within 27 to 56 days after Dose 4, and had no other major protocol deviations as determined by the clinician. Here, "Number of Subjects Analyzed" = number of participants with valid IgG concentrations for the specified serotype reported at 1 month after Dose 4.

End point type	Primary

End point timeframe:

1 month after Dose 4

End point values	20vPnC	13vPnC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	755	745		
Units: microgram per milliliter (µg/mL)				
geometric mean (confidence interval 95%)				
Serotype 1 (n=755, 744)	1.47 (1.37 to 1.57)	2.12 (1.97 to 2.27)		
Serotype 3 (n=755, 745)	0.56 (0.53 to 0.60)	0.85 (0.80 to 0.90)		
Serotype 4 (n=754, 745)	3.77 (3.52 to 4.04)	4.84 (4.50 to 5.22)		
Serotype 5 (n=755, 745)	1.87 (1.74 to 2.00)	2.51 (2.33 to 2.70)		
Serotype 6A (n=755, 745)	9.01 (8.45 to 9.61)	11.69 (10.91 to 12.53)		
Serotype 6B (n=753, 744)	4.01 (3.70 to 4.35)	5.74 (5.27 to 6.24)		
Serotype 7F (n=755, 745)	3.91 (3.70 to 4.14)	5.18 (4.88 to 5.49)		
Serotype 9V (n=755, 744)	3.44 (3.23 to 3.67)	4.30 (4.02 to 4.59)		
Serotype 14 (n=755, 745)	5.68 (5.27 to 6.12)	6.34 (5.88 to 6.83)		
Serotype 18C (n=755, 745)	3.46 (3.24 to 3.70)	4.69 (4.34 to 5.05)		
Serotype 19A (n=754, 745)	3.53 (3.30 to 3.77)	4.13 (3.84 to 4.45)		
Serotype 19F (n=755, 745)	5.01 (4.68 to 5.36)	5.79 (5.36 to 6.25)		
Serotype 23F (n=755, 745)	3.95 (3.63 to 4.31)	6.18 (5.66 to 6.75)		
Serotype 8 (n=755, 720)	3.97 (3.73 to 4.22)	0.03 (0.03 to 0.04)		
Serotype 10A (n=755, 744)	6.22 (5.75 to 6.72)	0.01 (0.01 to 0.01)		
Serotype 11A (n=755, 745)	3.53 (3.31 to 3.78)	0.02 (0.02 to 0.02)		
Serotype 12F (n=755, 745)	1.85 (1.73 to 1.99)	0.01 (0.01 to 0.01)		
Serotype 15B (n=755, 745)	12.59 (11.78 to 13.45)	0.02 (0.02 to 0.03)		
Serotype 22F (n=755, 745)	10.60 (9.92 to 11.33)	0.00 (0.00 to 0.01)		
Serotype 33F (n=755, 745)	9.31 (8.71 to 9.96)	0.01 (0.01 to 0.01)		

Statistical analyses

Statistical analysis title	NI of 20vPnC-13vPnC for 13 matched serotype

Statistical analysis description:

Serotype 5: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC-

13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution).

Comparison groups	20vPnC v 13vPnC
Number of subjects included in analysis	1500
Analysis specification	Pre-specified
Analysis type	non-inferiority[33]
Parameter estimate	Geometric Mean Ratio
Point estimate	0.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.67
upper limit	0.82

Notes:

[33] - Comparison for the 13 matched serotypes for 20vPnC was to the corresponding serotype in 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the IgG GMR of 20vPnC to 13vPnC for the serotype is greater than 0.5 (2-fold NI margin).

Statistical analysis title	NI of 20vPnC-13vPnC for 13 matched serotype

Statistical analysis description:

Serotype 4: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC-13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution).

Comparison groups	20vPnC v 13vPnC
Number of subjects included in analysis	1500
Analysis specification	Pre-specified
Analysis type	non-inferiority[34]
Parameter estimate	Geometric Mean Ratio
Point estimate	0.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	0.86

Notes:

[34] - Comparison for the 13 matched serotypes for 20vPnC was to the corresponding serotype in 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the IgG GMR of 20vPnC to 13vPnC for the serotype is greater than 0.5 (2-fold NI margin).

Statistical analysis title	NI of 20vPnC-13vPnC for 13 matched serotype

Statistical analysis description:

Serotype 3: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC-13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution).

Comparison groups	20vPnC v 13vPnC
Number of subjects included in analysis	1500
Analysis specification	Pre-specified
Analysis type	non-inferiority[35]
Parameter estimate	Geometric Mean Ratio
Point estimate	0.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.61
upper limit	0.73

Notes:

[35] - Comparison for the 13 matched serotypes for 20vPnC was to the corresponding serotype in 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the IgG GMR of 20vPnC to 13vPnC for the serotype is greater than 0.5 (2-fold NI margin).

Statistical analysis title	NI of 20vPnC-13vPnC for 13 matched serotype

Statistical analysis description:

Serotype 1: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC-13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution).

Comparison groups	20vPnC v 13vPnC
Number of subjects included in analysis	1500
Analysis specification	Pre-specified
Analysis type	non-inferiority[36]
Parameter estimate	Geometric Mean Ratio
Point estimate	0.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.63
upper limit	0.76

Notes:

[36] - Comparison for the 13 matched serotypes for 20vPnC was to the corresponding serotype in 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the IgG GMR of 20vPnC to 13vPnC for the serotype is greater than 0.5 (2-fold NI margin).

Statistical analysis title	NI of 20vPnC-13vPnC for 13 matched serotype

Statistical analysis description:

Serotype 6A: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC-13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution).

Comparison groups	20vPnC v 13vPnC
Number of subjects included in analysis	1500
Analysis specification	Pre-specified
Analysis type	non-inferiority[37]
Parameter estimate	Geometric Mean Ratio
Point estimate	0.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	0.85

Notes:

[37] - Comparison for the 13 matched serotypes for 20vPnC was to the corresponding serotype in 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the IgG GMR of 20vPnC to 13vPnC for the serotype is greater than 0.5 (2-fold NI margin).

Statistical analysis title	NI of 20vPnC-13vPnC for 13 matched serotype

Statistical analysis description:

Serotype 14: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC-13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution).

Comparison groups	20vPnC v 13vPnC

Number of subjects included in analysis	1500
Analysis specification	Pre-specified
Analysis type	non-inferiority[38]
Parameter estimate	Geometric Mean Ratio
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.81
upper limit	1

Notes:

[38] - Comparison for the 13 matched serotypes for 20vPnC was to the corresponding serotype in 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the IgG GMR of 20vPnC to 13vPnC for the serotype is greater than 0.5 (2-fold NI margin).

Statistical analysis title	NI of 20vPnC-13vPnC for 13 matched serotype

Statistical analysis description:

Serotype 9V: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC-13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution).

Comparison groups	20vPnC v 13vPnC
Number of subjects included in analysis	1500
Analysis specification	Pre-specified
Analysis type	non-inferiority[39]
Parameter estimate	Geometric Mean Ratio
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.73
upper limit	0.88

Notes:

[39] - Comparison for the 13 matched serotypes for 20vPnC was to the corresponding serotype in 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the IgG GMR of 20vPnC to 13vPnC for the serotype is greater than 0.5 (2-fold NI margin).

Statistical analysis title	NI of 20vPnC-13vPnC for 13 matched serotype

Statistical analysis description:

Serotype 7F: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC-13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution).

Comparison groups	20vPnC v 13vPnC
Number of subjects included in analysis	1500
Analysis specification	Pre-specified
Analysis type	non-inferiority[40]
Parameter estimate	Geometric Mean Ratio
Point estimate	0.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	0.82

Notes:

[40] - Comparison for the 13 matched serotypes for 20vPnC was to the corresponding serotype in 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the IgG GMR of 20vPnC to 13vPnC for the serotype is greater than 0.5 (2-fold NI margin).

Statistical analysis title	NI of 20vPnC-13vPnC for 13 matched serotype

Statistical analysis description:

Serotype 6B: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC-13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution).

Comparison groups	20vPnC v 13vPnC
Number of subjects included in analysis	1500
Analysis specification	Pre-specified
Analysis type	non-inferiority[41]
Parameter estimate	Geometric Mean Ratio
Point estimate	0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.62
upper limit	0.79

Notes:

[41] - Comparison for the 13 matched serotypes for 20vPnC was to the corresponding serotype in 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the IgG GMR of 20vPnC to 13vPnC for the serotype is greater than 0.5 (2-fold NI margin).

Statistical analysis title	NI of 20vPnC-13vPnC for 13 matched serotype

Statistical analysis description:

Serotype 18C: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC-13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution).

Comparison groups	20vPnC v 13vPnC
Number of subjects included in analysis	1500
Analysis specification	Pre-specified
Analysis type	non-inferiority[42]
Parameter estimate	Geometric Mean Ratio
Point estimate	0.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.67
upper limit	0.82

Notes:

[42] - Comparison for the 13 matched serotypes for 20vPnC was to the corresponding serotype in 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the IgG GMR of 20vPnC to 13vPnC for the serotype is greater than 0.5 (2-fold NI margin).

Statistical analysis title	NI of 20vPnC - 13vPnC for 7 additional serotype

Statistical analysis description:

Serotype 10A: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC - lowest 13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution).

Comparison groups	20vPnC v 13vPnC

Number of subjects included in analysis	1500
Analysis specification	Pre-specified
Analysis type	non-inferiority[43]
Parameter estimate	Geometric Mean Ratio
Point estimate	2.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.64
upper limit	3.26

Notes:

[43] - For the additional 7 serotypes, the compared results were from serotype 1 (13vPnC serotype with the lowest GMC, not including serotype 3) in the 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the GMR (20vPnC/lowest 13vPnC) was greater than 0.5 (2-fold criterion).

Statistical analysis title	NI of 20vPnC - 13vPnC for 7 additional serotype

Statistical analysis description:

Serotype 8: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC - lowest 13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution).

Comparison groups	20vPnC v 13vPnC
Number of subjects included in analysis	1500
Analysis specification	Pre-specified
Analysis type	non-inferiority[44]
Parameter estimate	Geometric Mean Ratio
Point estimate	1.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.71
upper limit	2.06

Notes:

[44] - For the additional 7 serotypes, the compared results were from serotype 1 (13vPnC serotype with the lowest GMC, not including serotype 3) in the 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the GMR (20vPnC/lowest 13vPnC) was greater than 0.5 (2-fold criterion).

Statistical analysis title	NI of 20vPnC-13vPnC for 13 matched serotype

Statistical analysis description:

Serotype 23F: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC-13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution).

Comparison groups	20vPnC v 13vPnC
Number of subjects included in analysis	1500
Analysis specification	Pre-specified
Analysis type	non-inferiority[45]
Parameter estimate	Geometric Mean Ratio
Point estimate	0.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.57
upper limit	0.72

Notes:

[45] - Comparison for the 13 matched serotypes for 20vPnC was to the corresponding serotype in 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the IgG GMR of 20vPnC to 13vPnC for the serotype is greater than 0.5 (2-fold NI margin).

Statistical analysis title	NI of 20vPnC-13vPnC for 13 matched serotype

Statistical analysis description:

Serotype 19F: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC-13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution).

Comparison groups	20vPnC v 13vPnC
Number of subjects included in analysis	1500
Analysis specification	Pre-specified
Analysis type	non-inferiority[46]
Parameter estimate	Geometric Mean Ratio
Point estimate	0.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.78
upper limit	0.96

Notes:

[46] - Comparison for the 13 matched serotypes for 20vPnC was to the corresponding serotype in 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the IgG GMR of 20vPnC to 13vPnC for the serotype is greater than 0.5 (2-fold NI margin).

Statistical analysis title	NI of 20vPnC-13vPnC for 13 matched serotype

Statistical analysis description:

Serotype 19A: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC-13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution).

Comparison groups	20vPnC v 13vPnC
Number of subjects included in analysis	1500
Analysis specification	Pre-specified
Analysis type	non-inferiority[47]
Parameter estimate	Geometric Mean Ratio
Point estimate	0.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.77
upper limit	0.94

Notes:

[47] - Comparison for the 13 matched serotypes for 20vPnC was to the corresponding serotype in 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the IgG GMR of 20vPnC to 13vPnC for the serotype is greater than 0.5 (2-fold NI margin).

Statistical analysis title	NI of 20vPnC - 13vPnC for 7 additional serotype

Statistical analysis description:

Serotype 15B: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC - lowest 13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution).

Comparison groups	20vPnC v 13vPnC

Number of subjects included in analysis	1500
Analysis specification	Pre-specified
Analysis type	non-inferiority[48]
Parameter estimate	Geometric Mean Ratio
Point estimate	5.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.39
upper limit	6.55

Notes:

[48] - For the additional 7 serotypes, the compared results were from serotype 5 (13vPnC serotype with the lowest GMC, not including serotype 3) in the 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the GMR (20vPnC/lowest 13vPnC) was greater than 0.5 (2-fold criterion).

Statistical analysis title	NI of 20vPnC - 13vPnC for 7 additional serotype

Statistical analysis description:

Serotype 12F: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC - lowest 13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution).

Comparison groups	20vPnC v 13vPnC
Number of subjects included in analysis	1500
Analysis specification	Pre-specified
Analysis type	non-inferiority[49]
Parameter estimate	Geometric Mean Ratio
Point estimate	0.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.79
upper limit	0.97

Notes:

[49] - For the additional 7 serotypes, the compared results were from serotype 5 (13vPnC serotype with the lowest GMC, not including serotype 3) in the 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the GMR (20vPnC/lowest 13vPnC) was greater than 0.5 (2-fold criterion).

Statistical analysis title	NI of 20vPnC - 13vPnC for 7 additional serotype

Statistical analysis description:

Serotype 11A: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC - lowest 13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution).

Comparison groups	20vPnC v 13vPnC
Number of subjects included in analysis	1500
Analysis specification	Pre-specified
Analysis type	non-inferiority[50]
Parameter estimate	Geometric Mean Ratio
Point estimate	1.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.51
upper limit	1.84

Notes:

[50] - For the additional 7 serotypes, the compared results were from serotype 5 (13vPnC serotype with the lowest GMC, not including serotype 3) in the 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the GMR (20vPnC/lowest 13vPnC) was greater than 0.5 (2-fold criterion).

Statistical analysis title	NI of 20vPnC - 13vPnC for 7 additional serotype

Statistical analysis description:

Serotype 22F: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC - lowest 13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution).

Comparison groups	20vPnC v 13vPnC
Number of subjects included in analysis	1500
Analysis specification	Pre-specified
Analysis type	non-inferiority[51]
Parameter estimate	Geometric Mean Ratio
Point estimate	5.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.54
upper limit	5.52

Notes:

[51] - For the additional 7 serotypes, the compared results were from serotype 5 (13vPnC serotype with the lowest GMC, not including serotype 3) in the 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the GMR (20vPnC/lowest 13vPnC) was greater than 0.5 (2-fold criterion).

Statistical analysis title	NI of 20vPnC - 13vPnC for 7 additional serotype

Statistical analysis description:

Serotype 33F: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC - lowest 13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution).

Comparison groups	20vPnC v 13vPnC
Number of subjects included in analysis	1500
Analysis specification	Pre-specified
Analysis type	non-inferiority[52]
Parameter estimate	Geometric Mean Ratio
Point estimate	4.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.99
upper limit	4.85

Notes:

[52] - For the additional 7 serotypes, the compared results were from serotype 5 (13vPnC serotype with the lowest GMC, not including serotype 3) in the 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the GMR (20vPnC/lowest 13vPnC) was greater than 0.5 (2-fold criterion).

Primary: Percentage of Subjects With Prespecified Antibody Levels to Specific Concomitant Vaccine Antigens 1 month After Dose 3

End point title	Percentage of Subjects With Prespecified Antibody Levels to Specific Concomitant Vaccine Antigens 1 month After Dose 3

End point description:

Concentration of antibody to diphtheria toxoid (predefined level ≥0.1 IU/mL), tetanus toxoid (predefined level ≥0.1 IU/mL), IgG antibodies to pertussis antigens (pertussis toxin, filamentous hemagglutinin and

pertactin, each with the predefined level as the 5th percentile observed in the 13vPnC group), hepatitis B antibody (in milli-international units per mL [mIU/mL]) (predefined level ≥10 mIU/mL), neutralizing antibody (NA) titers to poliovirus types 1, 2, and 3 (predefined level NA titer ≥1:8), Haemophilus influenzae type b (Hib) (≥0.15 µg/mL) were determined on subsets of sera collected at the immunogenicity time point 1 month after Dose 3. The antibody levels were measured by a validated multiplex Luminex immunoassay. The concomitant immune responses were measured on random subsets. Here, 'Number of Subjects Analysed' = number of participants with valid assay results for the specified antigen at 1 month after Dose 3.

End point type	Primary

End point timeframe:

1 month after Dose 3

End point values	20vPnC	13vPnC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	370	363		
Units: percentage of subjects				
number (confidence interval 95%)				
Diphtheria (n=370, 363)	93.5 (90.5 to 95.8)	97.8 (95.7 to 99.0)		
Tetanus (n=370, 363)	99.7 (98.5 to 100.0)	99.4 (98.0 to 99.9)		
Pertussis (PT) (n=370, 363)	94.9 (92.1 to 96.9)	95.0 (92.3 to 97.0)		
Pertussis (FHA) (n=370, 363)	95.7 (93.1 to 97.5)	95.0 (92.3 to 97.0)		
Pertussis (PRN) (n=370, 363)	93.8 (90.8 to 96.0)	95.0 (92.3 to 97.0)		
hepatitis B surface antigen (HBsAg) (n=118, 127)	100.0 (96.9 to 100.0)	100.0 (97.1 to 100.0)		
Poliovirus (Type 1) (n=111, 117)	100.0 (96.7 to 100.0)	100 (96.9 to 100.0)		
Poliovirus (Type 2) (n=115, 120)	100.0 (96.8 to 100.0)	99.2 (95.4 to 100.0)		
Poliovirus (Type 3) (n=115, 120)	100.0 (96.8 to 100.0)	100.0 (97.0 to 100.0)		
Hib ≥0.15 µg/mL (n=124, 125)	100.0 (97.1 to 100.0)	100.0 (97.1 to 100.0)		

Statistical analyses

Statistical analysis title	NI of 20vPnC-13vPnC for concomitant vaccine

Statistical analysis description:

Diphtheria: 2-Sided CI was calculated using the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage.

Comparison groups	20vPnC v 13vPnC
Number of subjects included in analysis	733
Analysis specification	Pre-specified
Analysis type	non-inferiority[53]
Parameter estimate	Percentage Difference
Point estimate	-4.3

Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.5
upper limit	-1.4

Notes:

[53] - Noninferiority was declared if the lower bound of the 2-sided 95% CI for the percentage differences (20vPnC - 13vPnC) was greater than -10%.

Statistical analysis title	NI of 20vPnC-13vPnC for concomitant vaccine

Statistical analysis description:

Tetanus: 2-Sided CI was calculated using the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage.

Comparison groups	20vPnC v 13vPnC
Number of subjects included in analysis	733
Analysis specification	Pre-specified
Analysis type	non-inferiority[54]
Parameter estimate	Percentage Difference
Point estimate	0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	1.7

Notes:

[54] - Noninferiority was declared if the lower bound of the 2-sided 95% CI for the percentage differences (20vPnC - 13vPnC) was greater than -10%.

Statistical analysis title	NI of 20vPnC-13vPnC for concomitant vaccine

Statistical analysis description:

Pertussis (PT): 2-Sided CI was calculated using the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage.

Comparison groups	20vPnC v 13vPnC
Number of subjects included in analysis	733
Analysis specification	Pre-specified
Analysis type	non-inferiority[55]
Parameter estimate	Percentage Difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.5
upper limit	3.1

Notes:

[55] - Noninferiority was declared if the lower bound of the 2-sided 95% CI for the percentage differences (20vPnC - 13vPnC) was greater than -10%.

Statistical analysis title	NI of 20vPnC-13vPnC for concomitant vaccine

Statistical analysis description:

Pertussis (FHA): 2-Sided CI was calculated using the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage.

Comparison groups	20vPnC v 13vPnC

Number of subjects included in analysis	733
Analysis specification	Pre-specified
Analysis type	non-inferiority[56]
Parameter estimate	Percentage Difference
Point estimate	0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.5
upper limit	3.9

Notes:

[56] - Noninferiority was declared if the lower bound of the 2-sided 95% CI for the percentage differences (20vPnC - 13vPnC) was greater than -10%.

Statistical analysis title	NI of 20vPnC-13vPnC for concomitant vaccine

Statistical analysis description:

Pertussis (PRN): 2-Sided CI was calculated using the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage.2-Sided CIs are calculated using the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage.

Comparison groups	20vPnC v 13vPnC
Number of subjects included in analysis	733
Analysis specification	Pre-specified
Analysis type	non-inferiority[57]
Parameter estimate	Percentage Difference
Point estimate	-1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.7
upper limit	2.2

Notes:

[57] - Noninferiority was declared if the lower bound of the 2-sided 95% CI for the percentage differences (20vPnC - 13vPnC) was greater than -10%.

Statistical analysis title	NI of 20vPnC-13vPnC for concomitant vaccine

Statistical analysis description:

Poliovirus (Type 2): 2-Sided CI was calculated using the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage.

Comparison groups	20vPnC v 13vPnC
Number of subjects included in analysis	733
Analysis specification	Pre-specified
Analysis type	non-inferiority[58]
Parameter estimate	Percentage Difference
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.4
upper limit	4.6

Notes:

[58] - Noninferiority was declared if the lower bound of the 2-sided 95% CI for the percentage differences (20vPnC - 13vPnC) was greater than -10%.

Statistical analysis title	NI of 20vPnC-13vPnC for concomitant vaccine

Statistical analysis description:

HBsAg: 2-Sided CI was calculated using the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage.

Comparison groups	20vPnC v 13vPnC
Number of subjects included in analysis	733
Analysis specification	Pre-specified
Analysis type	non-inferiority[59]
Parameter estimate	Percentage Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.2
upper limit	2.9

Notes:

[59] - Noninferiority was declared if the lower bound of the 2-sided 95% CI for the percentage differences (20vPnC - 13vPnC) was greater than -10%.

Statistical analysis title	NI of 20vPnC-13vPnC for concomitant vaccine

Statistical analysis description:

Poliovirus (Type 1): 2-Sided CI was calculated using the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage.

Comparison groups	20vPnC v 13vPnC
Number of subjects included in analysis	733
Analysis specification	Pre-specified
Analysis type	non-inferiority[60]
Parameter estimate	Percentage Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.4
upper limit	3.2

Notes:

[60] - Noninferiority was declared if the lower bound of the 2-sided 95% CI for the percentage differences (20vPnC - 13vPnC) was greater than -10%.

Statistical analysis title	NI of 20vPnC-13vPnC for concomitant vaccine

Statistical analysis description:

Poliovirus (Type 3): 2-Sided CI was calculated using the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage.

Comparison groups	20vPnC v 13vPnC
Number of subjects included in analysis	733
Analysis specification	Pre-specified
Analysis type	non-inferiority[61]
Parameter estimate	Percentage Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.2
upper limit	3.1

Notes:

[61] - Noninferiority was declared if the lower bound of the 2-sided 95% CI for the percentage differences (20vPnC - 13vPnC) was greater than -10%.

Statistical analysis title	NI of 20vPnC-13vPnC for concomitant vaccine

Statistical analysis description:

Hib (≥0.15 µg/mL): 2-Sided CI were calculated using the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage.

Comparison groups	20vPnC v 13vPnC
Number of subjects included in analysis	733
Analysis specification	Pre-specified
Analysis type	non-inferiority[62]
Parameter estimate	Percentage Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3
upper limit	3

Notes:

[62] - Noninferiority was declared if the lower bound of the 2-sided 95% CI for the percentage differences (20vPnC - 13vPnC) was greater than -10%.

Secondary: Serotype-specific IgG GMCs and GMRs at 1 Month After Dose 3

End point title	Serotype-specific IgG GMCs and GMRs at 1 Month After Dose 3

End point description:

Pneumococcal IgG antibody against each of the 20 pneumococcal serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F, 8, 10A, 11A, 12F, 15B, 22F and 33F) was measured using direct binding Luminex assay. Results were expressed as IgG concentrations. GMCs and 2-sided CIs were calculated by exponentiating the mean logarithm of the concentrations and the corresponding CIs based on the Student's t distribution. Dose 3 evaluable immunogenicity population: eligible subjects aged 42-98 days on Dose 1, received assigned vaccine, had valid determinate IgG concentration for at least 1 serotype 1 month post Dose 3, had blood collection within 27-56 days post Dose 3, had not received prohibited vaccines before the blood draw at 1 month post Dose 3, had no major protocol deviations. Here, 'Number of Subjects Analysed' = number of participants with valid IgG concentrations for the specified serotype reported at 1 month after Dose 3.

End point type	Secondary

End point timeframe:

1 month after Dose 3

End point values	20vPnC	13vPnC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	833	803		
Units: µg/mL				
geometric mean (confidence interval 95%)				
Serotype 1 (n=833, 802)	0.74 (0.70 to 0.79)	1.14 (1.06 to 1.22)		
Serotype 3 (n=833, 802)	0.36 (0.33 to 0.38)	0.51 (0.48 to 0.55)		
Serotype 4 (n=833, 802)	0.75 (0.70 to 0.81)	1.08 (1.00 to 1.17)		
Serotype 5 (n=833, 802)	0.66 (0.61 to 0.71)	0.96 (0.88 to 1.04)		

Serotype 6A (n=833, 802)	1.95 (1.81 to 2.10)	2.69 (2.48 to 2.92)		
Serotype 6B (n=831, 801)	0.61 (0.55 to 0.68)	1.02 (0.91 to 1.14)		
Serotype 7F (n=833, 802)	1.71 (1.62 to 1.81)	2.29 (2.16 to 2.43)		
Serotype 9V (n=833, 802)	0.87 (0.81 to 0.93)	1.21 (1.12 to 1.30)		
Serotype 14 (n=832, 802)	2.16 (2.01 to 2.33)	2.72 (2.51 to 2.95)		
Serotype 18C (n=833, 802)	1.31 (1.23 to 1.39)	1.71 (1.59 to 1.84)		
Serotype 19A (n=833, 802)	0.72 (0.67 to 0.76)	0.91 (0.85 to 0.97)		
Serotype 19F (n=833, 802)	1.59 (1.50 to 1.67)	2.00 (1.88 to 2.12)		
Serotype 23F (n=833, 802)	0.82 (0.75 to 0.90)	1.25 (1.14 to 1.37)		
Serotype 8 (n=833, 794)	1.80 (1.70 to 1.91)	0.02 (0.02 to 0.02)		
Serotype 10A (n=833, 803)	1.21 (1.09 to 1.33)	0.01 (0.01 to 0.01)		
Serotype 11A (n=833, 803)	1.39 (1.30 to 1.48)	0.02 (0.01 to 0.02)		
Serotype 12F (n=833, 803)	0.55 (0.50 to 0.60)	0.01 (0.01 to 0.01)		
Serotype 15B (n=833, 803)	4.40 (4.11 to 4.71)	0.03 (0.02 to 0.03)		
Serotype 22F (n=833, 803)	3.71 (3.45 to 3.99)	0.01 (0.00 to 0.01)		
Serotype 33F (n=833, 802)	1.49 (1.36 to 1.64)	0.02 (0.01 to 0.02)		

Statistical analyses

Statistical analysis title	NI of 20vPnC-13vPnC for 13 matched serotype

Statistical analysis description:

Serotype 1: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC-13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution).

Comparison groups	20vPnC v 13vPnC
Number of subjects included in analysis	1636
Analysis specification	Pre-specified
Analysis type	non-inferiority[63]
Parameter estimate	Geometric Mean Ratios
Point estimate	0.65
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.59
upper limit	0.72

Notes:

[63] - Comparison for the 13 matched serotypes for 20vPnC is to the corresponding serotype in 13vPnC group. Noninferiority was declared for if the lower bound of the 2-sided 95% CI for the IgG GMR of 20vPnC to 13vPnC for the serotype is greater than 0.5 (2-fold NI margin).

Statistical analysis title	NI of 20vPnC-13vPnC for 13 matched serotype

Statistical analysis description:

Serotype 3: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC-13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution).

Comparison groups	20vPnC v 13vPnC
Number of subjects included in analysis	1636
Analysis specification	Pre-specified
Analysis type	non-inferiority[64]
Parameter estimate	Geometric Mean Ratio
Point estimate	0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.64
upper limit	0.76

Notes:

[64] - Comparison for the 13 matched serotypes for 20vPnC is to the corresponding serotype in 13vPnC group. Noninferiority was declared for if the lower bound of the 2-sided 95% CI for the IgG GMR of 20vPnC to 13vPnC for the serotype is greater than 0.5 (2-fold NI margin).

Statistical analysis title	NI of 20vPnC-13vPnC for 13 matched serotype

Statistical analysis description:

Serotype 4: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC-13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution).

Comparison groups	20vPnC v 13vPnC
Number of subjects included in analysis	1636
Analysis specification	Pre-specified
Analysis type	non-inferiority[65]
Parameter estimate	Geometric Mean Ratio
Point estimate	0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.63
upper limit	0.78

Notes:

[65] - Comparison for the 13 matched serotypes for 20vPnC is to the corresponding serotype in 13vPnC group. Noninferiority was declared for if the lower bound of the 2-sided 95% CI for the IgG GMR of 20vPnC to 13vPnC for the serotype is greater than 0.5 (2-fold NI margin).

Statistical analysis title	NI of 20vPnC-13vPnC for 13 matched serotype

Statistical analysis description:

Serotype 5: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC-13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution).

Comparison groups	20vPnC v 13vPnC
Number of subjects included in analysis	1636
Analysis specification	Pre-specified
Analysis type	non-inferiority[66]
Parameter estimate	Geometric Mean Ratio
Point estimate	0.69

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.61
upper limit	0.77

Notes:

[66] - Comparison for the 13 matched serotypes for 20vPnC is to the corresponding serotype in 13vPnC group. Noninferiority was declared for if the lower bound of the 2-sided 95% CI for the IgG GMR of 20vPnC to 13vPnC for the serotype is greater than 0.5 (2-fold NI margin).

Statistical analysis title	NI of 20vPnC-13vPnC for 13 matched serotype

Statistical analysis description:

Serotype 6A: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC-13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution).

Comparison groups	20vPnC v 13vPnC
Number of subjects included in analysis	1636
Analysis specification	Pre-specified
Analysis type	non-inferiority[67]
Parameter estimate	Geometric Mean Ratio
Point estimate	0.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.65
upper limit	0.81

Notes:

[67] - Comparison for the 13 matched serotypes for 20vPnC is to the corresponding serotype in 13vPnC group. Noninferiority was declared for if the lower bound of the 2-sided 95% CI for the IgG GMR of 20vPnC to 13vPnC for the serotype is greater than 0.5 (2-fold NI margin).

Statistical analysis title	NI of 20vPnC-13vPnC for 13 matched serotype

Statistical analysis description:

Serotype 6B: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC-13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution).

Comparison groups	20vPnC v 13vPnC
Number of subjects included in analysis	1636
Analysis specification	Pre-specified
Analysis type	non-inferiority[68]
Parameter estimate	Geometric Mean Ratio
Point estimate	0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.51
upper limit	0.7

Notes:

[68] - Comparison for the 13 matched serotypes for 20vPnC is to the corresponding serotype in 13vPnC group. Noninferiority was declared for if the lower bound of the 2-sided 95% CI for the IgG GMR of 20vPnC to 13vPnC for the serotype is greater than 0.5 (2-fold NI margin).

Statistical analysis title	NI of 20vPnC-13vPnC for 13 matched serotype

Statistical analysis description:

Serotype 7F: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC-13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t

distribution).

Comparison groups	20vPnC v 13vPnC
Number of subjects included in analysis	1636
Analysis specification	Pre-specified
Analysis type	non-inferiority[69]
Parameter estimate	Geometric Mean Ratio
Point estimate	0.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.69
upper limit	0.81

Notes:

[69] - Comparison for the 13 matched serotypes for 20vPnC is to the corresponding serotype in 13vPnC group. Noninferiority was declared for if the lower bound of the 2-sided 95% CI for the IgG GMR of 20vPnC to 13vPnC for the serotype is greater than 0.5 (2-fold NI margin).

Statistical analysis title	NI of 20vPnC-13vPnC for 13 matched serotype

Statistical analysis description:

Serotype 9V: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC-13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution).

Comparison groups	20vPnC v 13vPnC
Number of subjects included in analysis	1636
Analysis specification	Pre-specified
Analysis type	non-inferiority[70]
Parameter estimate	Geometric Mean Ratio
Point estimate	0.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.65
upper limit	0.8

Notes:

[70] - Comparison for the 13 matched serotypes for 20vPnC is to the corresponding serotype in 13vPnC group. Noninferiority was declared for if the lower bound of the 2-sided 95% CI for the IgG GMR of 20vPnC to 13vPnC for the serotype is greater than 0.5 (2-fold NI margin).

Statistical analysis title	NI of 20vPnC-13vPnC for 13 matched serotype

Statistical analysis description:

Serotype 14: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC-13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution).

Comparison groups	20vPnC v 13vPnC
Number of subjects included in analysis	1636
Analysis specification	Pre-specified
Analysis type	non-inferiority[71]
Parameter estimate	Geometric Mean Ratio
Point estimate	0.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	0.89

Notes:

[71] - Comparison for the 13 matched serotypes for 20vPnC is to the corresponding serotype in 13vPnC group. Noninferiority was declared for if the lower bound of the 2-sided 95% CI for the IgG GMR of 20vPnC to 13vPnC for the serotype is greater than 0.5 (2-fold NI margin).

Statistical analysis title	NI of 20vPnC-13vPnC for 13 matched serotype

Statistical analysis description:

Serotype 18C: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC-13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution).

Comparison groups	20vPnC v 13vPnC
Number of subjects included in analysis	1636
Analysis specification	Pre-specified
Analysis type	non-inferiority[72]
Parameter estimate	Geometric Mean Ratio
Point estimate	0.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	0.84

Notes:

[72] - Comparison for the 13 matched serotypes for 20vPnC is to the corresponding serotype in 13vPnC group. Noninferiority was declared for if the lower bound of the 2-sided 95% CI for the IgG GMR of 20vPnC to 13vPnC for the serotype is greater than 0.5 (2-fold NI margin).

Statistical analysis title	NI of 20vPnC - 13vPnC for 7 additional serotype

Statistical analysis description:

Serotype 15B: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC - lowest 13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution).

Comparison groups	20vPnC v 13vPnC
Number of subjects included in analysis	1636
Analysis specification	Pre-specified
Analysis type	non-inferiority[73]
Parameter estimate	Geometric Mean Ratio
Point estimate	4.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.39
upper limit	5.3

Notes:

[73] - For the additional 7 serotypes, the compared results are from serotype 19A (13vPnC serotype with the lowest GMC, not including serotype 3) in the 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the GMR (20vPnC/lowest 13vPnC) was greater than 0.5 (2-fold criterion).

Statistical analysis title	NI of 20vPnC-13vPnC for 13 matched serotype

Statistical analysis description:

Serotype 19A: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC-13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution).

Comparison groups	20vPnC v 13vPnC

Number of subjects included in analysis	1636
Analysis specification	Pre-specified
Analysis type	non-inferiority[74]
Parameter estimate	Geometric Mean Ratio
Point estimate	0.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.72
upper limit	0.86

Notes:

[74] - Comparison for the 13 matched serotypes for 20vPnC is to the corresponding serotype in 13vPnC group. Noninferiority was declared for if the lower bound of the 2-sided 95% CI for the IgG GMR of 20vPnC to 13vPnC for the serotype is greater than 0.5 (2-fold NI margin).

Statistical analysis title	NI of 20vPnC-13vPnC for 13 matched serotype

Statistical analysis description:

Serotype 19F: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC-13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution).

Comparison groups	20vPnC v 13vPnC
Number of subjects included in analysis	1636
Analysis specification	Pre-specified
Analysis type	non-inferiority[75]
Parameter estimate	Geometric Mean Ratio
Point estimate	0.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.73
upper limit	0.86

Notes:

[75] - Comparison for the 13 matched serotypes for 20vPnC is to the corresponding serotype in 13vPnC group. Noninferiority was declared for if the lower bound of the 2-sided 95% CI for the IgG GMR of 20vPnC to 13vPnC for the serotype is greater than 0.5 (2-fold NI margin).

Statistical analysis title	NI of 20vPnC-13vPnC for 13 matched serotype

Statistical analysis description:

Serotype 23F: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC-13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution).

Comparison groups	20vPnC v 13vPnC
Number of subjects included in analysis	1636
Analysis specification	Pre-specified
Analysis type	non-inferiority[76]
Parameter estimate	Geometric Mean Ratio
Point estimate	0.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.58
upper limit	0.75

Notes:

[76] - Comparison for the 13 matched serotypes for 20vPnC is to the corresponding serotype in 13vPnC group. Noninferiority was declared for if the lower bound of the 2-sided 95% CI for the IgG GMR of 20vPnC to 13vPnC for the serotype is greater than 0.5 (2-fold NI margin).

Statistical analysis title	NI of 20vPnC - 13vPnC for 7 additional serotype

Statistical analysis description:

Serotype 8: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC - lowest 13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution).

Comparison groups	20vPnC v 13vPnC
Number of subjects included in analysis	1636
Analysis specification	Pre-specified
Analysis type	non-inferiority[77]
Parameter estimate	Geometric Mean Ratio
Point estimate	1.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.81
upper limit	2.16

Notes:

[77] - For the additional 7 serotypes, the compared results are from serotype 19A (13vPnC serotype with the lowest GMC, not including serotype 3) in the 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the GMR (20vPnC/lowest 13vPnC) was greater than 0.5 (2-fold criterion).

Statistical analysis title	NI of 20vPnC - 13vPnC for 7 additional serotype

Statistical analysis description:

Serotype 10A: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC - lowest 13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution).

Comparison groups	20vPnC v 13vPnC
Number of subjects included in analysis	1636
Analysis specification	Pre-specified
Analysis type	non-inferiority[78]
Parameter estimate	Geometric Mean Ratio
Point estimate	1.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.18
upper limit	1.49

Notes:

[78] - For the additional 7 serotypes, the compared results are from serotype 19A (13vPnC serotype with the lowest GMC, not including serotype 3) in the 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the GMR (20vPnC/lowest 13vPnC) was greater than 0.5 (2-fold criterion).

Statistical analysis title	NI of 20vPnC - 13vPnC for 7 additional serotype

Statistical analysis description:

Serotype 11A: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC - lowest 13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution).

Comparison groups	20vPnC v 13vPnC

Number of subjects included in analysis	1636
Analysis specification	Pre-specified
Analysis type	non-inferiority[79]
Parameter estimate	Geometric Mean Ratio
Point estimate	1.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.39
upper limit	1.67

Notes:

[79] - For the additional 7 serotypes, the compared results are from serotype 19A (13vPnC serotype with the lowest GMC, not including serotype 3) in the 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the GMR (20vPnC/lowest 13vPnC) was greater than 0.5 (2-fold criterion).

Statistical analysis title	NI of 20vPnC - 13vPnC for 7 additional serotype

Statistical analysis description:

Serotype 12F: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC - lowest 13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution).

Comparison groups	20vPnC v 13vPnC
Number of subjects included in analysis	1636
Analysis specification	Pre-specified
Analysis type	non-inferiority[80]
Parameter estimate	Geometric Mean Ratio
Point estimate	0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.54
upper limit	0.67

Notes:

[80] - For the additional 7 serotypes, the compared results are from serotype 19A (13vPnC serotype with the lowest GMC, not including serotype 3) in the 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the GMR (20vPnC/lowest 13vPnC) was greater than 0.5 (2-fold criterion).

Statistical analysis title	NI of 20vPnC - 13vPnC for 7 additional serotype

Statistical analysis description:

Serotype 22F: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC - lowest 13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution).

Comparison groups	20vPnC v 13vPnC
Number of subjects included in analysis	1636
Analysis specification	Pre-specified
Analysis type	non-inferiority[81]
Parameter estimate	Geometric Mean Ratio
Point estimate	4.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.68
upper limit	4.48

Notes:

[81] - For the additional 7 serotypes, the compared results are from serotype 19A (13vPnC serotype with the lowest GMC, not including serotype 3) in the 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the GMR (20vPnC/lowest 13vPnC) was greater than 0.5 (2-fold criterion).

Statistical analysis title	NI of 20vPnC - 13vPnC for 7 additional serotype

Statistical analysis description:

Serotype 33F: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC - lowest 13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution).

Comparison groups	20vPnC v 13vPnC
Number of subjects included in analysis	1636
Analysis specification	Pre-specified
Analysis type	non-inferiority[82]
Parameter estimate	Geometric Mean Ratio
Point estimate	1.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.46
upper limit	1.83

Notes:

[82] - For the additional 7 serotypes, the compared results are from serotype 19A (13vPnC serotype with the lowest GMC, not including serotype 3) in the 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the GMR (20vPnC/lowest 13vPnC) was greater than 0.5 (2-fold criterion).

Secondary: Percentage of Subjects With Predefined IgG Concentrations 1 Month After Dose 4

End point title	Percentage of Subjects With Predefined IgG Concentrations 1 Month After Dose 4

End point description:

Pre-specified levels of serotypes were as follows: for serotype 1, 3, 4, 6A, 7F, 9V, 14, 18C, 19F, 23F, 8, 10A, 11A, 12F, 15B, 22F, 33F: >=0.35 microgram per mL (mcg/mL), for serotype 5: >=0.23 mcg/mL, for serotype 6B: >=0.10 mcg/mL and for serotype 19A: >=0.12 mcg/mL. "Numbers of Subjects Analyzed" were the denominators and numbers of participants with an IgG concentration ≥ the predefined level for the given serotype were the numerator for the percentage calculations. 95% CI was based on the Clopper and Pearson method. Dose 4 evaluable immunogenicity population: eligible subjects aged 42-98 days on Dose 1, received 4 doses to which they were randomized, have at least 1 valid immunogenicity result within 27 to 56 days post Dose 4, and had no other major protocol deviations as determined by the clinician. Here, "Number of Subjects Analyzed" = number of participants with valid IgG concentrations for the specified serotype reported at 1 month after Dose 4.

End point type	Secondary

End point timeframe:

1 month after Dose 4

End point values	20vPnC	13vPnC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	755	745		
Units: percentage of subjects				
number (confidence interval 95%)				
Serotype 1 (n=755, 744)	94.3 (92.4 to 95.8)	97.2 (95.7 to 98.2)		

Serotype 3 (n=755, 745)	73.6 (70.3 to 76.8)	85.8 (83.1 to 88.2)		
Serotype 4 (n=754, 745)	98.9 (97.9 to 99.5)	99.1 (98.1 to 99.6)		
Serotype 5 (n=755, 745)	97.9 (96.6 to 98.8)	97.7 (96.4 to 98.7)		
Serotype 6A (n=755, 745)	99.5 (98.6 to 99.9)	99.7 (99.0 to 100.0)		
Serotype 6B (n=753, 744)	99.1 (98.1 to 99.6)	99.5 (98.6 to 99.9)		
Serotype 7F (n=755, 745)	99.5 (98.6 to 99.9)	99.9 (99.3 to 100.0)		
Serotype 9V (n=755, 744)	98.5 (97.4 to 99.3)	98.9 (97.9 to 99.5)		
Serotype 14 (n=755, 745)	98.9 (97.9 to 99.5)	99.5 (98.6 to 99.9)		
Serotype 18C (n=755, 745)	98.9 (97.9 to 99.5)	99.5 (98.6 to 99.9)		
Serotype 19A (n=754, 745)	99.9 (99.3 to 100.0)	99.7 (99.0 to 100.0)		
Serotype 19F (n=755, 745)	98.8 (97.7 to 99.5)	98.9 (97.9 to 99.5)		
Serotype 23F (n=755, 745)	97.2 (95.8 to 98.3)	98.1 (96.9 to 99.0)		
Serotype 8 (n=755, 720)	99.5 (98.6 to 99.9)	4.7 (3.3 to 6.5)		
Serotype 10A (n=755, 744)	97.7 (96.4 to 98.7)	2.0 (1.1 to 3.3)		
Serotype 11A (n=755, 745)	98.8 (97.7 to 99.5)	4.2 (2.8 to 5.9)		
Serotype 12F (n=755, 745)	95.2 (93.5 to 96.6)	0.3 (0.0 to 1.0)		
Serotype 15B (n=755, 745)	99.7 (99.0 to 100.0)	4.6 (3.2 to 6.3)		
Serotype 22F (n=755, 745)	99.6 (98.8 to 99.9)	1.5 (0.7 to 2.6)		
Serotype 33F (n=755, 745)	99.5 (98.6 to 99.9)	1.7 (0.9 to 3.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Serotype-specific opsonophagocytic activity (OPA) Geometric Mean Titers (GMTs) at 1 Month After Dose 3

End point title	Serotype-specific opsonophagocytic activity (OPA) Geometric Mean Titers (GMTs) at 1 Month After Dose 3

End point description:

OPA titers for the 20 pneumococcal serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F, 8, 10A, 11A, 12F, 15B, 22F, and 33F) were determined in randomized subsets of participants at 1 month after Dose 3. Results were expressed as OPA titers. GMTs and 2-sided CIs were calculated by exponentiating the mean logarithm of the concentrations and the corresponding CIs based on the Student's t distribution. Dose 3 evaluable immunogenicity population: eligible subjects aged 42-98 days on Dose 1, received the first 3 doses to which they were randomized, have at least 1 valid immunogenicity result within 27 to 56 days after Dose 3, and had no other major protocol deviations as determined by the clinician. Here, "Number of Subjects Analyzed" = number of participants with valid OPA titers for the specified serotype reported at 1 month after Dose 3.

End point type	Secondary

End point timeframe:
1 month after Dose 3

End point values	20vPnC	13vPnC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	103	113		
Units: Titers				
geometric mean (confidence interval 95%)				
Serotype 1 (n=103, 98)	26 (21 to 33)	34 (27 to 42)		
Serotype 3 (n=105, 97)	51 (43 to 61)	63 (53 to 76)		
Serotype 4 (n=97, 90)	339 (252 to 455)	280 (207 to 378)		
Serotype 5 (n=103, 98)	32 (27 to 39)	39 (32 to 47)		
Serotype 6A (n=104, 96)	910 (763 to 1084)	936 (757 to 1156)		
Serotype 6B (n=99, 91)	318 (242 to 419)	516 (409 to 651)		
Serotype 7F (n=91, 87)	1222 (1020 to 1465)	1149 (926 to 1424)		
Serotype 9V (n=94, 87)	661 (482 to 906)	594 (421 to 838)		
Serotype 14 (n=103 ,97)	415 (323 to 535)	420 (330 to 535)		
Serotype 18C (n=95, 87)	1153 (910 to 1460)	996 (754 to 1317)		
Serotype 19A (n=93, 84)	108 (78 to 149)	109 (79 to 151)		
Serotype 19F (n=102, 97)	84 (67 to 105)	116 (90 to 149)		
Serotype 23F (n=96, 86)	255 (186 to 350)	295 (215 to 406)		
Serotype 8 (n=100, 112)	665 (503 to 880)	18 (17 to 20)		
Serotype 10A (n=101, 109)	2558 (1869 to 3501)	37 (33 to 42)		
Serotype 11A (n=100, 108)	289 (212 to 395)	50 (46 to 55)		
Serotype 12F (n=92, 110)	7677 (5952 to 9901)	28 (24 to 33)		
Serotype 15B (n=97, 110)	1560 (1090 to 2233)	18 (16 to 22)		
Serotype 22F (n=97, 113)	6797 (5170 to 8936)	9 (9 to 9)		
Serotype 33F (n=85, 111)	7388 (4803 to 11365)	198 (177 to 220)		

Statistical analyses

No statistical analyses for this end point

Secondary: Serotype-specific OPA GMTs at 1 Month After Dose 4

End point title	Serotype-specific OPA GMTs at 1 Month After Dose 4

End point description:

OPA titers for the 20 pneumococcal serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F, 8, 10A, 11A, 12F, 15B, 22F, and 33F) were determined in randomized subsets of participants at 1 month after Dose 4. Results were expressed as OPA titers. GMTs and 2-sided CIs were calculated by exponentiating the mean logarithm of the concentrations and the corresponding CIs based on the Student's t distribution. Dose 4 evaluable immunogenicity population: eligible subjects aged 42-98 days on Dose 1, received all 4 doses as randomized, have at least 1 valid immunogenicity result within 27 to 56 days after Dose 4, and had no other major protocol deviations as determined by the clinician. Here, "Number of Subjects Analyzed" = number of participants with valid OPA titers for the specified serotype reported at 1 month after Dose 4.

End point type	Secondary

End point timeframe:

1 month after Dose 4

End point values	20vPnC	13vPnC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	99	103		
Units: Titers				
geometric mean (confidence interval 95%)				
Serotype 1 (n=94, 91)	36 (27 to 48)	66 (50 to 87)		
Serotype 3 (n=92, 88)	62 (49 to 78)	102 (86 to 120)		
Serotype 4 (n=85, 82)	621 (435 to 887)	961 (714 to 1294)		
Serotype 5 (n=94, 91)	55 (45 to 67)	69 (54 to 87)		
Serotype 6A (n=93, 91)	1384 (1092 to 1753)	1767 (1329 to 2348)		
Serotype 6B (n=92, 88)	666 (489 to 906)	1211 (861 to 1703)		
Serotype 7F (n=84, 81)	2022 (1673 to 2444)	2099 (1741 to 2531)		
Serotype 9V (n=85, 79)	2609 (1913 to 3558)	3210 (2500 to 4123)		
Serotype 14 (n=92, 91)	667 (523 to 850)	593 (462 to 761)		
Serotype 18C (n=84, 83)	1973 (1472 to 2643)	2425 (1914 to 3072)		
Serotype 19A (n=85, 78)	844 (622 to 1145)	1357 (1007 to 1829)		
Serotype 19F (n=93, 91)	246 (179 to 337)	373 (272 to 513)		
Serotype 23F (n=84, 77)	827 (554 to 1235)	1532 (1118 to 2100)		
Serotype 8 (n=89, 97)	1228 (901 to 1673)	26 (21 to 31)		
Serotype 10A (n=99, 102)	3674 (2746 to 4916)	57 (44 to 74)		
Serotype 11A (n=90, 89)	2728 (1975 to 3768)	69 (53 to 89)		
Serotype 12F (n=86, 103)	9320 (7037 to 12343)	31 (26 to 37)		
Serotype 15B (n=92, 100)	3035 (2138 to 4308)	23 (17 to 30)		
Serotype 22F (n=86, 101)	11077 (7956 to 15422)	15 (11 to 20)		

Serotype 33F (n=80, 97)	19216 (13193 to 27990)	363 (292 to 451)		

Statistical analyses

No statistical analyses for this end point

Secondary: Serotype-specific IgG Geometric Mean Fold Rise (GMFRs) From 1 Month After Dose 3 to Before Dose 4

End point title	Serotype-specific IgG Geometric Mean Fold Rise (GMFRs) From 1 Month After Dose 3 to Before Dose 4

End point description:

GMFR of pneumococcal 20vPnC serotypes included: 1, 3, 4, 5, 6A, 6B, 7F, 8, 9V, 10A, 11A, 12F, 14, 15B, 18C, 19A, 19F, 22F, 23F and 33F. The GMFR from 1 month after Dose 3 to before Dose 4 were reported from Dose 3 evaluable immunogenicity subjects. Here, "Number of Subjects Analyzed" = subject evaluable for this endpoint and with valid IgG concentrations at both timepoints for the specified serotype.

End point type	Secondary

End point timeframe:

1 month after Dose 3 to before Dose 4

End point values	20vPnC	13vPnC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	758	733		
Units: Fold rise				
geometric mean (confidence interval 95%)				
Serotype 1 (n=758, 733)	0.3 (0.3 to 0.3)	0.3 (0.2 to 0.3)		
Serotype 3 (n=758, 733)	0.2 (0.2 to 0.2)	0.2 (0.2 to 0.2)		
Serotype 4 (n=758, 733)	0.3 (0.3 to 0.4)	0.3 (0.3 to 0.3)		
Serotype 5 (n=758, 733)	0.3 (0.3 to 0.3)	0.3 (0.3 to 0.3)		
Serotype 6A (n=758, 732)	0.3 (0.3 to 0.3)	0.3 (0.3 to 0.3)		
Serotype 6B (n=754, 730)	0.4 (0.4 to 0.4)	0.3 (0.3 to 0.3)		
Serotype 7F (n=758, 733)	0.4 (0.4 to 0.6)	0.4 (0.3 to 0.4)		
Serotype 9V (n=758, 733)	0.3 (0.3 to 0.4)	0.3 (0.3 to 0.3)		
Serotype 14 (n=757, 733)	0.5 (0.4 to 0.5)	0.5 (0.4 to 0.5)		
Serotype 18C (n=758, 733)	0.2 (0.2 to 0.2)	0.2 (0.2 to 0.2)		
Serotype 19A (n=757, 733)	0.2 (0.2 to 0.2)	0.2 (0.2 to 0.2)		
Serotype 19F (n=758, 733)	0.2 (0.2 to 0.3)	0.2 (0.2 to 0.2)		
Serotype 23F (n=758, 733)	0.3 (0.3 to 0.3)	0.3 (0.2 to 0.3)		
Serotype 8 (n=758, 706)	0.2 (0.2 to 0.3)	1.4 (1.3 to 1.5)		
Serotype 10A (n=758, 732)	0.7 (0.6 to 0.7)	0.9 (0.9 to 1.0)		
Serotype 11A (n=758, 732)	0.3 (0.2 to 0.3)	1.1 (1.0 to 1.2)		
Serotype 12F (n=758, 732)	0.3 (0.3 to 0.4)	1.0 (1.0 to 1.1)		
Serotype 15B (n=758, 732)	0.4 (0.3 to 0.4)	0.8 (0.7 to 0.8)		
Serotype 22F (n=758, 732)	0.3 (0.3 to 0.4)	0.8 (0.7 to 0.9)		
Serotype 33F (n=758, 731)	0.7 (0.7 to 0.8)	0.8 (0.7 to 0.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Serotype-specific IgG GMFRs From 1 Month Before to 1 month After Dose 4

End point title	Serotype-specific IgG GMFRs From 1 Month Before to 1 month After Dose 4

End point description:

GMFR of pneumococcal 20vPnC serotypes included: 1, 3, 4, 5, 6A, 6B, 7F, 8, 9V, 10A, 11A, 12F, 14, 15B, 18C, 19A, 19F, 22F, 23F and 33F. The GMFR from 1 month before Dose 4 to 1 month after Dose 4 were reported from Dose 4 evaluable immunogenicity subjects. Here "Number of Subjects Analyzed" = subject evaluable for this endpoint and with valid IgG concentrations at both timepoints for the specified serotype.

End point type	Secondary

End point timeframe:

From 1 month before to 1 month after Dose 4

End point values	20vPnC	13vPnC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	732	721		
Units: Fold rise				
geometric mean (confidence interval 95%)				
Serotype 1 (n=732, 720)	7.3 (6.9 to 7.8)	7.1 (6.7 to 7.6)		
Serotype 3 (n=732, 721)	8.5 (7.9 to 9.1)	9.0 (8.4 to 9.6)		
Serotype 4 (n=731, 721)	15.4 (14.3 to 16.6)	14.2 (13.1 to 15.3)		
Serotype 6A (n=732, 720)	15.2 (14.3 to 16.2)	14.5 (13.5 to 15.5)		
Serotype 6B (n=727, 718)	18.0 (16.8 to 19.3)	17.0 (15.8 to 18.2)		
Serotype 7F (n=732, 721)	6.0 (5.7 to 6.3)	6.4 (6.0 to 6.8)		
Serotype 9V (n=732, 720)	11.8 (11.1 to 12.6)	11.2 (10.5 to 11.9)		
Serotype 14 (n=732, 721)	5.9 (5.4 to 6.3)	5.0 (4.6 to 5.3)		
Serotype 5 (n=732, 721)	8.9 (8.4 to 9.5)	8.5 (8.0 to 9.0)		
Serotype 18C (n=732, 721)	11.3 (10.6 to 12.0)	11.4 (10.7 to 12.1)		
Serotype 19A (n=731, 721)	25.6 (23.8 to 27.6)	25.6 (23.6 to 27.7)		
Serotype 19F (n=732, 721)	13.1 (12.2 to 14.1)	12.5 (11.6 to 13.5)		
Serotype 23F (n=732, 721)	18.1 (16.8 to 19.5)	19.2 (17.9 to 20.6)		
Serotype 8 (n=732, 692)	9.1 (8.5 to 9.8)	1.3 (1.2 to 1.4)		
Serotype 10A (n=732, 718)	8.1 (7.6 to 8.7)	1.1 (1.0 to 1.1)		

Serotype 11A (n=732, 719)	9.8 (9.1 to 10.6)	1.1 (1.0 to 1.2)		
Serotype 12F (n=732, 719)	10.0 (9.4 to 10.6)	1.0 (1.0 to 1.1)		
Serotype 15B (n=732, 719)	8.1 (7.5 to 8.7)	1.2 (1.2 to 1.3)		
Serotype 22F (n=732, 719)	8.4 (7.9 to 9.1)	1.2 (1.1 to 1.3)		
Serotype 33F (n=732, 719)	8.8 (8.2 to 9.4)	1.1 (1.0 to 1.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Serotype-specific IgG GMFRs From 1 Month After Dose 3 to 1 Month After Dose 4

End point title	Serotype-specific IgG GMFRs From 1 Month After Dose 3 to 1 Month After Dose 4

End point description:

GMFR of pneumococcal 20vPnC serotypes included: 1, 3, 4, 5, 6A, 6B, 7F, 8, 9V, 10A, 11A, 12F, 14, 15B, 18C, 19A, 19F, 22F, 23F and 33F. The GMFR from 1 month after Dose 3 to 1 month after Dose 4 were reported from subjects in both Dose 3 and Dose 4 evaluable immunogenicity populations. Here, "Number of Subjects Analyzed" = subject evaluable for this endpoint and with valid IgG concentrations at both timepoints for the specified serotype.

End point type	Secondary

End point timeframe:

from 1 month after Dose 3 to 1 month after Dose 4

End point values	20vPnC	13vPnC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	704	687		
Units: Fold rise				
geometric mean (confidence interval 95%)				
Serotype 1 (n=704, 685)	2.0 (1.9 to 2.1)	1.8 (1.7 to 1.9)		
Serotype 3 (n=704, 686)	1.6 (1.5 to 1.7)	1.7 (1.6 to 1.8)		
Serotype 4 (n=703, 686)	5.1 (4.8 to 5.5)	4.4 (4.1 to 4.8)		
Serotype 5 (n=704, 686)	2.9 (2.7 to 3.1)	2.6 (2.4 to 2.8)		
Serotype 6A (n=704, 686)	4.7 (4.4 to 5.0)	4.3 (4.0 to 4.6)		
Serotype 6B (n=700, 685)	6.8 (6.2 to 7.4)	5.5 (5.0 to 6.0)		
Serotype 7F (n=704, 686)	2.3 (2.2 to 2.4)	2.2 (2.1 to 2.3)		
Serotype 9V (n=704, 685)	4.0 (3.7 to 4.3)	3.4 (3.2 to 3.7)		
Serotype 14 (n=703, 686)	2.6 (2.4 to 2.9)	2.2 (2.0 to 2.5)		
Serotype 18C (n=704, 686)	2.7 (2.5 to 2.8)	2.6 (2.5 to 2.8)		
Serotype 19A (n=703, 686)	4.9 (4.6 to 5.2)	4.6 (4.2 to 4.9)		
Serotype 19F (n=704, 686)	3.2 (3.0 to 3.4)	2.9 (2.7 to 3.1)		
Serotype 23F (n=704, 686)	4.9 (4.5 to 5.3)	4.9 (4.5 to 5.3)		
Serotype 8 (n=704, 659)	2.2 (2.0 to 2.3)	1.8 (1.6 to 2.0)		
Serotype 10A (n=704, 686)	5.3 (4.9 to 5.8)	1.0 (0.9 to 1.1)		
Serotype 11A (n=704, 687)	2.6 (2.4 to 2.8)	1.1 (1.0 to 1.3)		
Serotype 12F (n=704, 687)	3.3 (3.1 to 3.6)	1.0 (1.0 to 1.1)		

Serotype 15B (n=704, 687)	2.8 (2.6 to 3.0)	1.0 (0.9 to 1.1)		
Serotype 22F (n=704, 687)	2.9 (2.7 to 3.1)	1.0 (0.9 to 1.1)		
Serotype 33F (n=704, 686)	6.4 (5.9 to 7.0)	0.8 (0.8 to 0.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Alternative Prespecified Hib Antibody Level 1 Month After Dose 3

End point title	Percentage of Subjects With Alternative Prespecified Hib Antibody Level 1 Month After Dose 3

End point description:

Antibody concentration to the Hib vaccine antigens were determined on sera collected from randomly selected subsets of participants with sufficient sera volumes. Percentage of subjects with alternative prespecified Hib antibody (≥1.0 µg/mL) were reported from Dose 3 evaluable immunogenicity subjects. Subjects analyzed were restricted to those participants who received the appropriate concomitant vaccines with the first 3 doses. Here, "Number of Subjects Analyzed" = number of participants with valid Hib antibody level for the specified antigen.

End point type	Secondary

End point timeframe:

1 month after Dose 3

End point values	20vPnC	13vPnC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	124	125		
Units: percentage of subjects				
number (confidence interval 95%)				
≥1.0 µg/mL	75.0 (66.4 to 82.3)	72.0 (63.3 to 79.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Ratios (GMRs) of Prespecified Antibody Levels to Specific Concomitant Vaccine Antigens 1 month after Dose 4

End point title	Geometric Mean Ratios (GMRs) of Prespecified Antibody Levels to Specific Concomitant Vaccine Antigens 1 month after Dose 4

End point description:

Antibody concentrations to each concomitant vaccine antigen (measles, mumps, rubella, and varicella) were determined on sera collected 1 month after Dose 4 from a randomly selected subset of participants with sufficient sera volumes. GMs and 2-sided CIs were calculated by exponentiating the mean logarithm of the concentrations and the corresponding CIs based on the Student's t distribution and were reported from Dose 4 evaluable immunogenicity subjects. Dose 4 evaluable immunogenicity population restricted to those who received the corresponding concomitant vaccine with the specified concomitant vaccine antigen. Here, "Number of Subjects Analyzed" = number of participants with valid antibody concentrations for the specified antigen reported at 1 month after Dose 4.

End point type	Secondary

End point timeframe:

1 month after Dose 4

End point values	20vPnC	13vPnC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	234	232		
Units: see the table below				
geometric mean (confidence interval 95%)				
Measles (AU/mL) (n=234, 232)	277.74 (243.88 to 316.30)	215.41 (184.61 to 251.35)		
Mumps (AU/mL) (n=234, 232)	36.96 (30.82 to 44.33)	34.19 (28.94 to 40.39)		
Rubella (IU/mL) (n=234, 232)	49.63 (43.88 to 56.13)	40.44 (35.19 to 46.48)		
Varicella (mIU/mL) (n=231, 229)	233.05 (207.25 to 262.06)	234.78 (208.84 to 263.94)		

Statistical analyses

Statistical analysis title	NI of 20vPnc-13vPnC for vaccine antigen

Statistical analysis description:

Measles: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC - 13vPnC) of the logarithms of the concentrations and the corresponding CI (based on the Student's t distribution).

Comparison groups	20vPnC v 13vPnC
Number of subjects included in analysis	466
Analysis specification	Pre-specified
Analysis type	non-inferiority[83]
Parameter estimate	Geometric Mean Ratios
Point estimate	1.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.05
upper limit	1.58

Notes:

[83] - Noninferiority was declared if the lower bound of the 2-sided 95% CI for the GMR of 20vPnC group to 13vPnC group is greater than 0.5 (2-fold NI margin).

Statistical analysis title	NI of 20vPnc-13vPnC for vaccine antigen

Statistical analysis description:

Varicella: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC - 13vPnC) of the logarithms of the concentrations and the corresponding CI (based on the Student's t distribution).

Comparison groups	20vPnC v 13vPnC

Number of subjects included in analysis	466
Analysis specification	Pre-specified
Analysis type	non-inferiority[84]
Parameter estimate	Geometric Mean Ratios
Point estimate	0.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.84
upper limit	1.17

Notes:

[84] - Noninferiority was declared if the lower bound of the 2-sided 95% CI for the GMR of 20vPnC group to 13vPnC group is greater than 0.5 (2-fold NI margin).

Statistical analysis title	NI of 20vPnc-13vPnC for vaccine antigen

Statistical analysis description:

Rubella: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC - 13vPnC) of the logarithms of the concentrations and the corresponding CI (based on the Student's t distribution).

Comparison groups	20vPnC v 13vPnC
Number of subjects included in analysis	466
Analysis specification	Pre-specified
Analysis type	non-inferiority[85]
Parameter estimate	Geometric Mean Ratios
Point estimate	1.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.02
upper limit	1.48

Notes:

[85] - Noninferiority was declared if the lower bound of the 2-sided 95% CI for the GMR of 20vPnC group to 13vPnC group is greater than 0.5 (2-fold NI margin).

Statistical analysis title	NI of 20vPnc-13vPnC for vaccine antigen

Statistical analysis description:

Mumps: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC - 13vPnC) of the logarithms of the concentrations and the corresponding CI (based on the Student's t distribution).

Comparison groups	20vPnC v 13vPnC
Number of subjects included in analysis	466
Analysis specification	Pre-specified
Analysis type	non-inferiority[86]
Parameter estimate	Geometric Mean Ratios
Point estimate	1.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.85
upper limit	1.38

Notes:

[86] - Noninferiority was declared if the lower bound of the 2-sided 95% CI for the GMR of 20vPnC group to 13vPnC group is greater than 0.5 (2-fold NI margin).

Adverse events

Adverse events information

Timeframe for reporting adverse events:

LR and SE [systematic assessment(SA)]:within 7 days after Dose 1, 2, 3, 4; SAEs: from Dose 1 up to 6 months after Dose 4; other AEs [non-systematic assessment (non-SA)]:from Dose 1 up to 1 month after Dose 3 and from Dose 4 up to 1 month after Dose 4

Adverse event reporting additional description:

Same events may appear as both an AE and a SAE. However, what are presented are distinct events. An event may be classified as serious in 1 subject and as non-serious in another subject, or 1 subject may have experienced both a SAE and non-SAE during the study

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups

Reporting group title	13vPnC

Reporting group description:

Infants 42 to 98 days of age were enrolled to receive 4 doses of 0.5 millilitre (mL) 13-valent Pneumococcal Conjugate Vaccine (13vPnC) intramuscularly. Dose 1 was given at enrollment and Dose 2 and 3 were given 42 to 63 days from the previous dose. Dose 4 was administered at 365 to 455 days of age.

Reporting group title	20vPnC

Reporting group description:

Infants 42 to 98 days of age were enrolled to receive 4 doses of 0.5 millilitre (mL) 20-valent Pneumococcal Conjugate Vaccine (20vPnC) intramuscularly. Dose 1 was given at enrollment and Dose 2 and 3 were given 42 to 63 days from the previous dose. Dose 4 was administered at 365 to 455 days of age.

Serious adverse events	13vPnC	20vPnC	
Total subjects affected by serious adverse events			
subjects affected / exposed	31 / 987 (3.14%)	45 / 1001 (4.50%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Thermal burn			
subjects affected / exposed	1 / 987 (0.10%)	0 / 1001 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haematoma			
subjects affected / exposed	0 / 987 (0.00%)	1 / 1001 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skull fracture			

subjects affected / exposed	0 / 987 (0.00%)	1 / 1001 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	0 / 987 (0.00%)	1 / 1001 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Extradural haematoma			
subjects affected / exposed	0 / 987 (0.00%)	1 / 1001 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Accidental poisoning			
subjects affected / exposed	1 / 987 (0.10%)	0 / 1001 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Accidental exposure to product			
subjects affected / exposed	0 / 987 (0.00%)	1 / 1001 (0.10%)	
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	0 / 987 (0.00%)	1 / 1001 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Partial seizures			
subjects affected / exposed	1 / 987 (0.10%)	0 / 1001 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemic seizure			
subjects affected / exposed	1 / 987 (0.10%)	0 / 1001 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile convulsion			

subjects affected / exposed	2 / 987 (0.20%)	2 / 1001 (0.20%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Status epilepticus			
subjects affected / exposed	1 / 987 (0.10%)	0 / 1001 (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			
Systemic inflammatory response syndrome			
subjects affected / exposed	0 / 987 (0.00%)	1 / 1001 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Immune thrombocytopenia			
subjects affected / exposed	0 / 987 (0.00%)	1 / 1001 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia			
subjects affected / exposed	0 / 987 (0.00%)	1 / 1001 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Microcytic anaemia			
subjects affected / exposed	1 / 987 (0.10%)	0 / 1001 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	0 / 987 (0.00%)	1 / 1001 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intussusception			

subjects affected / exposed	1 / 987 (0.10%)	0 / 1001 (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			
Acute respiratory failure			
subjects affected / exposed	1 / 987 (0.10%)	0 / 1001 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthma			
subjects affected / exposed	1 / 987 (0.10%)	0 / 1001 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bullous impetigo			
subjects affected / exposed	0 / 987 (0.00%)	1 / 1001 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchiolitis			
subjects affected / exposed	4 / 987 (0.41%)	4 / 1001 (0.40%)	
occurrences causally related to treatment / all	0 / 4	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenovirus infection			
subjects affected / exposed	0 / 987 (0.00%)	1 / 1001 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dengue fever			
subjects affected / exposed	0 / 987 (0.00%)	1 / 1001 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	1 / 987 (0.10%)	0 / 1001 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cellulitis			
subjects affected / exposed	0 / 987 (0.00%)	1 / 1001 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronavirus infection			
subjects affected / exposed	0 / 987 (0.00%)	1 / 1001 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Croup infectious			
subjects affected / exposed	0 / 987 (0.00%)	1 / 1001 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia necrotising			
subjects affected / exposed	1 / 987 (0.10%)	0 / 1001 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 987 (0.10%)	2 / 1001 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metapneumovirus bronchiolitis			
subjects affected / exposed	1 / 987 (0.10%)	0 / 1001 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hand-foot-and-mouth disease			
subjects affected / exposed	1 / 987 (0.10%)	1 / 1001 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Groin abscess			
subjects affected / exposed	0 / 987 (0.00%)	1 / 1001 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal viral infection			

subjects affected / exposed	0 / 987 (0.00%)	1 / 1001 (0.10%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis norovirus			
subjects affected / exposed	0 / 987 (0.00%)	1 / 1001 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	5 / 987 (0.51%)	0 / 1001 (0.00%)	
occurrences causally related to treatment / all	0 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia urinary tract infection			
subjects affected / exposed	2 / 987 (0.20%)	0 / 1001 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia respiratory syncytial viral			
subjects affected / exposed	0 / 987 (0.00%)	1 / 1001 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus infection			
subjects affected / exposed	2 / 987 (0.20%)	5 / 1001 (0.50%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus bronchiolitis			
subjects affected / exposed	3 / 987 (0.30%)	7 / 1001 (0.70%)	
occurrences causally related to treatment / all	0 / 3	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			
subjects affected / exposed	0 / 987 (0.00%)	1 / 1001 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection viral			

subjects affected / exposed	1 / 987 (0.10%)	0 / 1001 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 987 (0.00%)	1 / 1001 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection pseudomonal			
subjects affected / exposed	1 / 987 (0.10%)	0 / 1001 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			
subjects affected / exposed	1 / 987 (0.10%)	1 / 1001 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media acute			
subjects affected / exposed	0 / 987 (0.00%)	1 / 1001 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Failure to thrive			
subjects affected / exposed	1 / 987 (0.10%)	2 / 1001 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	1 / 987 (0.10%)	2 / 1001 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	13vPnC	20vPnC	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	939 / 987 (95.14%)	966 / 1001 (96.50%)	
Nervous system disorders			
Hypersomnia (INCREASED SLEEP)			
alternative assessment type: Systematic			
subjects affected / exposed	798 / 987 (80.85%)	823 / 1001 (82.22%)	
occurrences (all)	2268	2309	
General disorders and administration site conditions			
Pyrexia (FEVER)			
alternative assessment type: Systematic			
subjects affected / exposed	314 / 987 (31.81%)	322 / 1001 (32.17%)	
occurrences (all)	504	550	
Injection site swelling (SWELLING)			
subjects affected / exposed	359 / 987 (36.37%)	353 / 1001 (35.26%)	
occurrences (all)	707	635	
Injection site pain (PAIN)			
subjects affected / exposed	663 / 987 (67.17%)	689 / 1001 (68.83%)	
occurrences (all)	1543	1634	
Injection site erythema (REDNESS)			
subjects affected / exposed	492 / 987 (49.85%)	498 / 1001 (49.75%)	
occurrences (all)	986	944	
Psychiatric disorders			
Irritability (IRRITABILITY)			
alternative assessment type: Systematic			
subjects affected / exposed	863 / 987 (87.44%)	894 / 1001 (89.31%)	
occurrences (all)	3301	3380	
Infections and infestations			
Otitis media			
subjects affected / exposed	50 / 987 (5.07%)	56 / 1001 (5.59%)	
occurrences (all)	65	73	
Upper respiratory tract infection			
subjects affected / exposed	112 / 987 (11.35%)	114 / 1001 (11.39%)	
occurrences (all)	137	137	

Metabolism and nutrition disorders			
Decreased appetite (DECREASED APPETITE)			
alternative assessment type: Systematic			
subjects affected / exposed	492 / 987 (49.85%)	521 / 1001 (52.05%)	
occurrences (all)	1028	1041	

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