Clinical trial results:
A Phase 3, Single-arm Trial to Evaluate the Safety and Immunogenicity of a 20-Valent Pneumococcal Conjugate Vaccine in Healthy Children 15 Months Through 17 Years of Age

Summary

EudraCT number	2019-003308-11
Trial protocol	Outside EU/EEA
Global end of trial date	06 April 2022

Results information

Result version number	v2 (current)
This version publication date	06 March 2024
First version publication date	24 September 2022
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	B7471014

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04642079
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 ClinicalTrials.gov Call Center, Pfizer Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-002330-PIP01-18
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 July 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	06 April 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To describe the safety profile of 20-valent pneumococcal conjugate (20vPnC).
Cohort 1 (subjects aged >=15 to <24 months) and Cohort 2 (subjects aged >=2 to <5 years): To demonstrate that the serotype-specific immunoglobulin G (IgG) concentrations for the 7 additional serotypes 1 month after 20-valent pneumococcal conjugate (20vPnC) are superior to the corresponding IgG concentrations before 20vPnC.
Cohort 3 (subjects aged >=5 to <10 years) and Cohort 4 (subjects aged >=10 to <18 years): To demonstrate that the serotype-specific opsonophagocytic activity (OPA) titers for the 7 additional serotypes 1 month after 20vPnC are superior to the corresponding OPA titers before 20vPnC.

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	04 December 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 839
Worldwide total number of subjects	839
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)	210
Children (2-11 years)	473
Adolescents (12-17 years)	156

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 839 subjects were enrolled and assigned to receive a single dose of 20vPnC of which 8 subjects were not vaccinated and 831 were vaccinated with 20vPnC.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1: 20vPnC: >=15 to <24 Months

Arm description:

Subjects aged >=15 months to <24 months who have been previously vaccinated with at least 3 doses of 13vPnC, were administered a single dose of 0.5 millilitre (mL) 20vPnC intramuscularly on Day 1.

Arm type	Experimental
Investigational medicinal product name	20-Valent Pneumococcal Conjugate Vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects were administered a single 0.5 mL dose of 20vPnC intramuscularly on Day 1.

Arm title	Cohort 2: 20vPnC: >=2 to <5 Years

Arm description:

Subjects aged >=2 to <5 years who have been previously vaccinated with at least 3 doses of 13vPnC, were administered a single dose of 0.5 mL 20vPnC intramuscularly on Day 1.

Arm type	Experimental
Investigational medicinal product name	20-Valent Pneumococcal Conjugate Vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects were administered a single 0.5 mL dose of 20vPnC intramuscularly on Day 1.

Arm title	Cohort 3: 20vPnC: >=5 to <10 Years

Arm description:

Subjects aged >=5 to <10 years regardless of previous vaccination status with 7vPnC or 13vPnC, were administered a single dose of 0.5 mL 20vPnC intramuscularly into the left arm on Day 1.

Arm type	Experimental
Investigational medicinal product name	20-Valent Pneumococcal Conjugate Vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects were administered a single 0.5 mL dose of 20vPnC intramuscularly on Day 1.

Arm title	Cohort 4: 20vPnC: >=10 to <18 Years

Arm description:

Subjects aged >=10 to <18 years regardless of previous vaccination status with 7vPnC or 13vPnC, were administered a single dose of 0.5 mL 20vPnC intramuscularly into the left arm on Day 1.

Arm type	Experimental
Investigational medicinal product name	20-Valent Pneumococcal Conjugate Vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects were administered a single 0.5 mL dose of 20vPnC intramuscularly on Day 1.

Number of subjects in period 1	Cohort 1: 20vPnC: >=15 to <24 Months	Cohort 2: 20vPnC: >=2 to <5 Years	Cohort 3: 20vPnC: >=5 to <10 Years
Started	210	219	203
Vaccinated	209	216	201
Completed	207	210	199
Not completed	3	9	4
No longer meets eligibility criteria	1	-	1
Not specified	-	-	-
Lost to follow-up	2	5	2
Consent withdrawn by parent/guardian/subject	-	4	1

Number of subjects in period 1	Cohort 4: 20vPnC: >=10 to <18 Years
Started	207
Vaccinated	205
Completed	203
Not completed	4
No longer meets eligibility criteria	1
Not specified	1
Lost to follow-up	-
Consent withdrawn by parent/guardian/subject	2

Baseline characteristics

Reporting groups	
Reporting group title	Cohort 1: 20vPnC: >=15 to <24 Months
Reporting group description:	
Subjects aged >=15 months to <24 months who have been previously vaccinated with at least 3 doses of 13vPnC, were administered a single dose of 0.5 millilitre (mL) 20vPnC intramuscularly on Day 1.	
Reporting group title	Cohort 2: 20vPnC: >=2 to <5 Years
Reporting group description:	
Subjects aged >=2 to <5 years who have been previously vaccinated with at least 3 doses of 13vPnC, were administered a single dose of 0.5 mL 20vPnC intramuscularly on Day 1.	
Reporting group title	Cohort 3: 20vPnC: >=5 to <10 Years
Reporting group description:	
Subjects aged >=5 to <10 years regardless of previous vaccination status with 7vPnC or 13vPnC, were administered a single dose of 0.5 mL 20vPnC intramuscularly into the left arm on Day 1.	
Reporting group title	Cohort 4: 20vPnC: >=10 to <18 Years
Reporting group description:	
Subjects aged >=10 to <18 years regardless of previous vaccination status with 7vPnC or 13vPnC, were administered a single dose of 0.5 mL 20vPnC intramuscularly into the left arm on Day 1.	

Reporting group values	Cohort 1: 20vPnC: >=15 to <24 Months	Cohort 2: 20vPnC: >=2 to <5 Years	Cohort 3: 20vPnC: >=5 to <10 Years
Number of subjects	210	219	203
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23months)	210	0	0
Children (2-11 years)	0	219	203
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous			
Age is reported in Months for 'Cohort 1: 20vPnC: >=15 to <24 Months'			
Units: years			
arithmetic mean	18.3	3.0	7.2
standard deviation	± 2.67	± 0.82	± 1.38
Sex: Female, Male Units: Subjects			
Female	93	111	94
Male	117	108	109
Race Units: Subjects			
American Indian or Alaska Native	0	1	0
Asian	3	0	0
Native Hawaiian or Other Pacific Islander	0	0	0

Black or African American	26	26	22
White	169	175	176
More than one race	10	14	5
Unknown or Not Reported	2	3	0
Ethnicity Units: Subjects			
Hispanic or Latino	35	46	32
Not Hispanic or Latino	173	173	169
Unknown or Not Reported	2	0	2

Reporting group values	Cohort 4: 20vPnC: >=10 to <18 Years	Total	
Number of subjects	207	839	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23months)	0	210	
Children (2-11 years)	51	473	
Adolescents (12-17 years)	156	156	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Age Continuous			
Age is reported in Months for 'Cohort 1: 20vPnC: >=15 to <24 Months'			
Units: years			
arithmetic mean	13.6		
standard deviation	± 2.32	-	
Sex: Female, Male Units: Subjects			
Female	91	389	
Male	116	450	
Race Units: Subjects			
American Indian or Alaska Native	0	1	
Asian	0	3	
Native Hawaiian or Other Pacific Islander	1	1	
Black or African American	17	91	
White	180	700	
More than one race	9	38	
Unknown or Not Reported	0	5	
Ethnicity Units: Subjects			
Hispanic or Latino	45	158	
Not Hispanic or Latino	161	676	
Unknown or Not Reported	1	5	

End points

End points reporting groups

Reporting group title	Cohort 1: 20vPnC: >=15 to <24 Months
Reporting group description:	
Subjects aged >=15 months to <24 months who have been previously vaccinated with at least 3 doses of 13vPnC, were administered a single dose of 0.5 millilitre (mL) 20vPnC intramuscularly on Day 1.	
Reporting group title	Cohort 2: 20vPnC: >=2 to <5 Years
Reporting group description:	
Subjects aged >=2 to <5 years who have been previously vaccinated with at least 3 doses of 13vPnC, were administered a single dose of 0.5 mL 20vPnC intramuscularly on Day 1.	
Reporting group title	Cohort 3: 20vPnC: >=5 to <10 Years
Reporting group description:	
Subjects aged >=5 to <10 years regardless of previous vaccination status with 7vPnC or 13vPnC, were administered a single dose of 0.5 mL 20vPnC intramuscularly into the left arm on Day 1.	
Reporting group title	Cohort 4: 20vPnC: >=10 to <18 Years
Reporting group description:	
Subjects aged >=10 to <18 years regardless of previous vaccination status with 7vPnC or 13vPnC, were administered a single dose of 0.5 mL 20vPnC intramuscularly into the left arm on Day 1.	

Primary: Percentage of Subjects Reporting Prompted Local Reactions Within 7 Days After Vaccination

End point title	Percentage of Subjects Reporting Prompted Local Reactions Within 7 Days After Vaccination[1]
End point description:	
Local reactions included pain at injection site, redness and swelling recorded by parent's/legal guardian's of subjects in an electronic diary (e-diary). Redness and swelling were measured and recorded in measuring device units. One measuring device unit =0.5 centimetre (cm). Redness and swelling were graded as mild: greater than (>) 0.0 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 (cohort 1) and did not interfere with activity (cohort 2-4); moderate: hurt if gently touched with crying (cohort 1) and interfered with daily activity (cohort 2-4) and; severe: limited limb movement (cohort 1) and prevented daily activity (cohort 2-4). 95 percent (%) confidence interval (CI) was based on Clopper and Pearson method. Safety population included all subjects who received 20vPnC and had safety follow-up after vaccination. Here, "Number of Subjects Analysed" signifies subjects evaluable for this endpoint.	
End point type	Primary
End point timeframe:	
Within 7 days after vaccination	
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: No statistical analysis were performed.	

End point values	Cohort 1: 20vPnC: >=15 to <24 Months	Cohort 2: 20vPnC: >=2 to <5 Years	Cohort 3: 20vPnC: >=5 to <10 Years	Cohort 4: 20vPnC: >=10 to <18 Years
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	204	215	199	205
Units: Percentage of subjects				
number (confidence interval 95%)				
Redness: Any	37.7 (31.1 to 44.8)	39.1 (32.5 to 45.9)	37.2 (30.5 to 44.3)	15.1 (10.5 to 20.8)
Redness: Mild	30.4 (24.2 to 37.2)	22.8 (17.4 to 29.0)	16.6 (11.7 to 22.5)	10.7 (6.8 to 15.8)

Redness: Moderate	7.4 (4.2 to 11.8)	15.3 (10.8 to 20.9)	18.6 (13.4 to 24.7)	3.9 (1.7 to 7.5)
Redness: Severe	0 (0.0 to 1.8)	0.9 (0.1 to 3.3)	2.0 (0.6 to 5.1)	0.5 (0.0 to 2.7)
Swelling: Any	22.1 (16.6 to 28.4)	23.3 (17.8 to 29.5)	27.1 (21.1 to 33.9)	15.6 (10.9 to 21.3)
Swelling: Mild	15.7 (11.0 to 21.4)	11.6 (7.7 to 16.7)	10.6 (6.7 to 15.7)	5.4 (2.7 to 9.4)
Swelling: Moderate	6.4 (3.4 to 10.7)	11.2 (7.3 to 16.2)	15.6 (10.8 to 21.4)	10.2 (6.5 to 15.2)
Swelling: Severe	0 (0.0 to 1.8)	0.5 (0.0 to 2.6)	1.0 (0.1 to 3.6)	0 (0.0 to 1.8)
Pain at injection site: Any	52.5 (45.4 to 59.5)	66.0 (59.3 to 72.3)	82.9 (77.0 to 87.9)	82.0 (76.0 to 87.0)
Pain at injection site: Mild	41.7 (34.8 to 48.8)	47.0 (40.2 to 53.9)	56.8 (49.6 to 63.8)	62.9 (55.9 to 69.6)
Pain at the injection site: Moderate	9.8 (6.1 to 14.7)	17.7 (12.8 to 23.4)	24.6 (18.8 to 31.2)	17.6 (12.6 to 23.5)
Pain at the injection site: Severe	1.0 (0.1 to 3.5)	1.4 (0.3 to 4.0)	1.5 (0.3 to 4.3)	1.5 (0.3 to 4.2)

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Reporting Prompted Systemic Events Within 7 Days After Vaccination: Cohort 1

End point title	Percentage of Subjects Reporting Prompted Systemic Events Within 7 Days After Vaccination: Cohort 1[2][3]

End point description:

Systemic events for Cohort 1 were recorded by parents/legal guardians of subject's using an e-diary. Fever was defined as temperature greater than or equal to (>=) 38.0 degree Celsius (C) and categorised as >=38.0 to 38.4 degree C, >38.4 to 38.9 degree C, >38.9 to 40.0 degree C and >40.0 degree 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). 95% CI was based on Clopper and Pearson method. Safety population included all subjects who received 20vPnC and had safety follow-up after vaccination. "Number of Subjects Analysed" = subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Within 7 days after vaccination

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: This endpoint was planned to be analysed only for the specified reporting arms.
[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analysed only for the specified reporting arms.

End point values	Cohort 1: 20vPnC: >=15 to <24 Months			
Subject group type	Reporting group			
Number of subjects analysed	204			
Units: Percentage of subjects				
number (confidence interval 95%)				
Fever: =>38.0 degree C	11.8 (7.7 to 17.0)			
Fever: =>38.0 degree C to 38.4 degree C	5.9 (3.1 to 10.0)			
Fever: >38.4 degree C to 38.9 degree C	2.9 (1.1 to 6.3)			
Fever: >38.9 degree C to 40.0 degree C	2.9 (1.1 to 6.3)			
Fever: >40.0 degree C	0 (0.0 to 1.8)			
Decreased appetite: Any	25.0 (19.2 to 31.5)			
Decreased appetite: Mild	17.6 (12.7 to 23.6)			
Decreased appetite: Moderate	6.4 (3.4 to 10.7)			
Decreased appetite: Severe	1.0 (0.1 to 3.5)			
Drowsiness/increased sleep: Any	41.7 (34.8 to 48.8)			
Drowsiness/increased sleep: Mild	31.4 (25.1 to 38.2)			
Drowsiness/increased sleep: Moderate	9.3 (5.7 to 14.2)			
Drowsiness/increased sleep: Severe	1.0 (0.1 to 3.5)			
Irritability: Any	61.8 (54.7 to 68.5)			
Irritability: Mild	22.5 (17.0 to 28.9)			
Irritability: Moderate	37.3 (30.6 to 44.3)			
Irritability: Severe	2.0 (0.5 to 4.9)			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Reporting Prompted Systemic Events Within 7 Days After Vaccination: Cohorts 2, 3 and 4

End point title	Percentage of Subjects Reporting Prompted Systemic Events Within 7 Days After Vaccination: Cohorts 2, 3 and 4[4][5]

End point description:

Systemic events for Cohort 2-4 included fever, fatigue, headache, muscle pain and joint pain, recorded by parents/legal guardians of subject's using an e-diary. Fever was defined as temperature >=38.0 degree C and categorised as >=38.0 to 38.4 degree C,>38.4 to 38.9 degree C,>38.9 to 40.0 degree C and >40.0 degree C. Fatigue, headache, muscle pain and joint pain were graded as mild (no interference with activity), moderate (some interference with activity) and severe (prevents daily routine activity). 95% CI was based on Clopper and Pearson method. Safety population included all subjects who received 20vPnC and had safety follow-up after vaccination. "Number of Subjects Analysed" = subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Within 7 days after vaccination

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: No statistical analysis were performed.

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analysed only for the specified reporting arms.

End point values	Cohort 2: 20vPnC: >=2 to <5 Years	Cohort 3: 20vPnC: >=5 to <10 Years	Cohort 4: 20vPnC: >=10 to <18 Years	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	215	199	205	
Units: Percentage of subjects				
number (confidence interval 95%)				
Fever: =>38.0 degree C	3.3 (1.3 to 6.6)	0.5 (0.0 to 2.8)	0 (0.0 to 1.8)	
Fever: =>38.0 degree C to 38.4 degree C	1.4 (0.3 to 4.0)	0.5 (0.0 to 2.8)	0 (0.0 to 1.8)	
Fever: 38.4 degree C to 38.9 degree C	1.4 (0.3 to 4.0)	0 (0.0 to 1.8)	0 (0.0 to 1.8)	
Fever: 38.9 degree C to 40.0 degree C	0.5 (0.0 to 2.6)	0 (0.0 to 1.8)	0 (0.0 to 1.8)	
Fever: =>40.0 degree C	0 (0.0 to 1.7)	0 (0.0 to 1.8)	0 (0.0 to 1.8)	
Fatigue: Any	37.2 (30.7 to 44.0)	28.1 (22.0 to 34.9)	27.8 (21.8 to 34.5)	
Fatigue: Mild	21.9 (16.5 to 28.0)	19.1 (13.9 to 25.3)	15.6 (10.9 to 21.3)	
Fatigue: Moderate	14.4 (10.0 to 19.8)	8.5 (5.1 to 13.3)	12.2 (8.0 to 17.5)	
Fatigue: Severe	0.9 (0.1 to 3.3)	0.5 (0.0 to 2.8)	0 (0.0 to 1.8)	
Headache: Any	5.6 (2.9 to 9.5)	18.6 (13.4 to 24.7)	29.3 (23.1 to 36.0)	
Headache: Mild	3.3 (1.3 to 6.6)	14.6 (10.0 to 20.3)	20.0 (14.8 to 26.1)	
Headache: Moderate	1.9 (0.5 to 4.7)	3.0 (1.1 to 6.4)	7.8 (4.5 to 12.4)	
Headache: Severe	0.5 (0.0 to 2.6)	1.0 (0.1 to 3.6)	1.5 (0.3 to 4.2)	
Muscle pain: Any	26.5 (20.7 to 32.9)	39.2 (32.4 to 46.3)	48.3 (41.3 to 55.4)	
Muscle pain: Mild	17.7 (12.8 to 23.4)	26.6 (20.6 to 33.3)	34.6 (28.1 to 41.6)	
Muscle pain: Moderate	8.4 (5.0 to 12.9)	11.1 (7.1 to 16.3)	13.2 (8.9 to 18.6)	
Muscle pain: Severe	0.5 (0.0 to 2.6)	1.5 (0.3 to 4.3)	0.5 (0.0 to 2.7)	
Joint pain: Any	3.7 (1.6 to 7.2)	6.5 (3.5 to 10.9)	8.3 (4.9 to 12.9)	
Joint pain: Mild	2.3 (0.8 to 5.3)	3.0 (1.1 to 6.4)	3.4 (1.4 to 6.9)	
Joint pain: Moderate	1.4 (0.3 to 4.0)	3.0 (1.1 to 6.4)	4.9 (2.4 to 8.8)	
Joint pain: Severe	0 (0.0 to 1.7)	0.5 (0.0 to 2.8)	0 (0.0 to 1.8)	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Reporting Adverse Events (AEs) up to 1 Month After Vaccination

End point title	Percentage of Subjects Reporting Adverse Events (AEs) up to 1 Month After Vaccination[6]

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. 95% CI was based on the Clopper and Pearson method. Safety population included all subjects who received 20vPnC and had safety follow-up after vaccination.

End point type	Primary

End point timeframe:

From Day 1 of vaccination up to 1 month after vaccination

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: No statistical analysis were performed.

End point values	Cohort 1: 20vPnC: >=15 to <24 Months	Cohort 2: 20vPnC: >=2 to <5 Years	Cohort 3: 20vPnC: >=5 to <10 Years	Cohort 4: 20vPnC: >=10 to <18 Years
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	209	216	201	205
Units: Percentage of subjects				
number (confidence interval 95%)	23.9 (18.3 to 30.3)	7.9 (4.7 to 12.3)	6.5 (3.5 to 10.8)	4.4 (2.0 to 8.2)

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Reporting Serious Adverse Events (SAEs) up to 6 Months After Vaccination

End point title	Percentage of Subjects Reporting Serious Adverse Events (SAEs) up to 6 Months After Vaccination[7]

End point description:

An SAE was any untoward medical occurrence that occurred, at any dose: resulted in death; required inpatient hospitalisation or prolongation of existing hospitalisation; was life-threatening; resulted in persistent or significant disability/ incapacity; was a congenital anomaly/birth defect and other important medical events. 95% CI was based on the Clopper and Pearson method. Safety population included all subjects who received 20vPnC and had safety follow-up after vaccination.

End point type	Primary

End point timeframe:

From Day 1 of vaccination up to 6 months after vaccination

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: No statistical analysis were performed.

End point values	Cohort 1: 20vPnC: >=15 to <24 Months	Cohort 2: 20vPnC: >=2 to <5 Years	Cohort 3: 20vPnC: >=5 to <10 Years	Cohort 4: 20vPnC: >=10 to <18 Years
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	209	216	201	205
Units: Percentage of subjects				
number (confidence interval 95%)	0.5 (0.0 to 2.6)	0 (0.0 to 1.7)	0 (0.0 to 1.8)	1.5 (0.3 to 4.2)

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Reporting Newly Diagnosed Chronic Medical Conditions (NDCMCs) up to 6 Months After Vaccination

End point title	Percentage of Subjects Reporting Newly Diagnosed Chronic Medical Conditions (NDCMCs) up to 6 Months After Vaccination[8]

End point description:

An NDCMC was defined as a disease or medical condition, not previously identified, that was expected to be persistent or was otherwise long-lasting in its effects. 95% CI was based on the Clopper and Pearson method. Safety population included all subjects who received 20vPnC and had safety follow-up after vaccination.

End point type	Primary

End point timeframe:

From Day 1 of vaccination up to 6 months after vaccination

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: No statistical analysis were performed.

End point values	Cohort 1: 20vPnC: >=15 to <24 Months	Cohort 2: 20vPnC: >=2 to <5 Years	Cohort 3: 20vPnC: >=5 to <10 Years	Cohort 4: 20vPnC: >=10 to <18 Years
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	209	216	201	205
Units: Percentage of subjects				
number (confidence interval 95%)	3.3 (1.4 to 6.8)	0.5 (0.0 to 2.6)	0.5 (0.0 to 2.7)	1.0 (0.1 to 3.5)

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Fold Rises (GMFRs) of Pneumococcal Serotype-Specific Immunoglobulin G (IgG) Concentrations for the 7 Additional Serotypes From Before to 1 Month After 20vPnC Vaccination: Cohort 1 and 2

End point title	Geometric Mean Fold Rises (GMFRs) of Pneumococcal Serotype-Specific Immunoglobulin G (IgG) Concentrations for the 7 Additional Serotypes From Before to 1 Month After 20vPnC Vaccination: Cohort 1 and 2[9][10]

End point description:

Pneumococcal serotype-specific IgG concentrations were measured from serum samples for 7 additional 20vPnC serotypes: 8, 10A, 11A, 12F, 15B, 22F and 33F. GMFR=geometric mean of fold rise from before vaccination on Day 1 to 1 month after vaccination with 20vPnC. GMFRs and corresponding 2-sided CIs were calculated by exponentiating the mean logarithm of titres or fold rises and the corresponding CIs (based on Student t distribution). Superiority of IgG concentration 1 month after 20vPnC to before vaccination for each serotype was demonstrated if the 95% lower CI of GMFR was >1. Evaluable

immunogenicity population (EIP) included all subjects who were eligible; received 20vPnC; at least 1 valid immunogenicity result from 1 month after vaccination collected within 27 to 56 days after vaccination for Cohorts 1-2; no other major protocol deviations. Number of Subjects Analysed=subjects included in the EIP and n=subjects with valid assay results at both timepoints for the specified serotype.

End point type	Primary

End point timeframe:

Before vaccination to 1 month after vaccination

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: This endpoint was planned to be analysed only for the specified reporting arms.

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analysed only for the specified reporting arms.

End point values	Cohort 1: 20vPnC: >=15 to <24 Months	Cohort 2: 20vPnC: >=2 to <5 Years		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	190	183		
Units: Fold rise				
geometric mean (confidence interval 95%)				
Serotype 8 (n=186, 178)	113.4 (93.2 to 137.9)	107.0 (86.1 to 133.0)		
Serotype 10A (n=188, 181)	83.2 (69.1 to 100.2)	106.7 (86.2 to 132.0)		
Serotype 11A (n=188, 182)	62.7 (49.9 to 78.8)	43.6 (33.2 to 57.1)		
Serotype 12F (n=188, 182)	27.9 (22.9 to 34.1)	36.6 (30.1 to 44.7)		
Serotype 15B (n=188, 180)	52.1 (43.2 to 62.8)	73.3 (58.7 to 91.5)		
Serotype 22F (n=188, 182)	1847.7 (1481.3 to 2304.5)	796.2 (577.1 to 1098.4)		
Serotype 33F (n=188, 182)	113.5 (92.5 to 139.2)	78.3 (61.6 to 99.5)		

Statistical analyses

No statistical analyses for this end point

Primary: GMFRs of Pneumococcal Serotype-Specific Opsonophagocytic Activity (OPA) Titres for the 7 Additional Serotypes From Before to 1 Month After 20PnC Vaccination: Cohort 3 and 4

End point title	GMFRs of Pneumococcal Serotype-Specific Opsonophagocytic Activity (OPA) Titres for the 7 Additional Serotypes From Before to 1 Month After 20PnC Vaccination: Cohort 3 and 4[11][12]

End point description:

Pneumococcal serotype-specific OPA titers were measured from serum samples for 7 additional 20vPnC serotypes: 8, 10A, 11A, 12F, 15B, 22F and 33F. GMFR was calculated as geometric mean of fold rise from before vaccination on Day 1 to 1 month after vaccination with 20vPnC. GMFRs and the corresponding 2-sided CIs were calculated by exponentiating the mean logarithm of the titres or fold rises and the corresponding CIs (based on the Student t distribution). Superiority of OPA titers 1 month

after 20vPnC to before vaccination for each serotype was demonstrated if the 95% lower CI of the GMFR was >1. EIP included all subjects who were eligible; received 20vPnC; at least 1 valid immunogenicity result from 1 month after vaccination collected within 27 to 49 days after vaccination for Cohorts 3-4; no other major protocol deviations. Here, Number of Subjects Analysed=subjects included in the EIP and n=subjects with valid assay results at both timepoints for the specified serotype.

End point type	Primary

End point timeframe:

Before vaccination to 1 month after vaccination

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: This endpoint was planned to be analysed only for the specified reporting arms.
[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analysed only for the specified reporting arms.

End point values	Cohort 3: 20vPnC: >=5 to <10 Years	Cohort 4: 20vPnC: >=10 to <18 Years		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	186	198		
Units: Fold rise				
geometric mean (confidence interval 95%)				
Serotype 8 (n=153, 174)	106.5 (79.9 to 142.0)	86.3 (64.2 to 115.9)		
Serotype 10A (n=134, 142)	30.6 (20.1 to 46.6)	33.5 (22.3 to 50.1)		
Serotype 11A (n=136, 155)	11.6 (7.6 to 17.7)	14.9 (10.2 to 21.8)		
Serotype 12F (n=154, 164)	463.6 (332.3 to 646.7)	454.1 (333.3 to 618.7)		
Serotype 15B (n=142, 164)	380.8 (228.3 to 635.2)	499.0 (338.7 to 735.3)		
Serotype 22F (n=137, 168)	128.5 (76.7 to 215.3)	111.2 (67.1 to 184.3)		
Serotype 33F (n=144, 158)	14.2 (10.9 to 18.4)	11.5 (8.9 to 14.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Predefined Levels of Pneumococcal Serotype-Specific IgG Concentrations for the 7 Additional Serotypes at 1 Month After Vaccination in Cohort 1 Only

End point title	Percentage of Subjects With Predefined Levels of Pneumococcal Serotype-Specific IgG Concentrations for the 7 Additional Serotypes at 1 Month After Vaccination in Cohort 1 Only[13]

End point description:

Pneumococcal serotype-specific IgG concentrations were measured from serum samples for 7 additional 20vPnC serotypes: 8, 10A, 11A, 12F, 15B, 22F and 33F. Percentage of subjects with predefined level (>=0.35 micrograms per millilitre (mcg/mL) of IgG concentration for the 7 additional 20vPnC serotypes was presented. 95% CI was based on Clopper and Pearson method. EIP included all subjects who were eligible; received 20vPnC; at least 1 valid immunogenicity result from 1 month after vaccination

collected within 27 to 56 days after vaccination for Cohort 1; no other major protocol deviations. Here, "Number of Subjects Analysed" signifies subjects included in the EIP with valid assay results.

End point type	Secondary

End point timeframe:

At 1 Month after vaccination

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analysed only for the specified reporting arms.

End point values	Cohort 1: 20vPnC: >=15 to <24 Months			
Subject group type	Reporting group			
Number of subjects analysed	190			
Units: Percentage of subjects				
number (confidence interval 95%)				
Serotype 8	100.0 (98.1 to 100.0)			
Serotype 10A	83.2 (77.1 to 88.2)			
Serotype 11A	93.2 (88.6 to 96.3)			
Serotype 12F	40.0 (33.0 to 47.3)			
Serotype 15B	83.7 (77.6 to 88.6)			
Serotype 22F	98.9 (96.2 to 99.9)			
Serotype 33F	92.6 (87.9 to 95.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Concentrations (GMCs) of Pneumococcal Serotype-Specific IgG for the 20vPnC Serotypes Before and 1 Month After Vaccination

End point title	Geometric Mean Concentrations (GMCs) of Pneumococcal Serotype-Specific IgG for the 20vPnC Serotypes Before and 1 Month After Vaccination

End point description:

Pneumococcal serotype-specific IgG concentrations were measured for serum samples for 13vPnC serotypes: 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F; and 7 additional 20vPnC serotypes: 8, 10A, 11A, 12F, 15B, 22F and 33F. GMCs were calculated by exponentiating the mean logarithm of the concentrations and the corresponding CIs (based on the Student t distribution). EIP included all subjects who were eligible; received 20vPnC; at least 1 valid immunogenicity result from 1 month after vaccination collected within 27 to 56 days or within 27 to 49 days after vaccination for Cohorts 1-2 or Cohorts 3-4, respectively; no other major protocol deviations. Here, "Number of Subjects Analysed" signifies subjects included in the EIP and n=subjects with valid IgG concentrations at the specified timepoint.

End point type	Secondary

End point timeframe:

Before vaccination (Vacc.) and 1 month after vaccination (1M after Vacc.)

End point values	Cohort 1: 20vPnC: >=15 to <24 Months	Cohort 2: 20vPnC: >=2 to <5 Years	Cohort 3: 20vPnC: >=5 to <10 Years	Cohort 4: 20vPnC: >=10 to <18 Years
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	190	183	186	198
Units: Micrograms per millilitre				
geometric mean (confidence interval 95%)				
Before Vacc.,Serotype 1 (n=189,183,186,198)	0.43 (0.37 to 0.49)	0.20 (0.17 to 0.24)	0.12 (0.10 to 0.14)	0.09 (0.08 to 0.11)
1M after Vacc.,Serotype 1 (n=190,183,186,198)	1.46 (1.28 to 1.67)	4.21 (3.62 to 4.90)	5.86 (5.15 to 6.67)	4.04 (3.32 to 4.93)
Before Vacc.,Serotype 3 (n=189,183,186,198)	0.14 (0.12 to 0.16)	0.08 (0.06 to 0.10)	0.22 (0.17 to 0.30)	0.15 (0.11 to 0.20)
1M after Vacc.,Serotype 3 (n=190,183,186,198)	0.54 (0.47 to 0.61)	1.21 (1.04 to 1.42)	1.32 (1.16 to 1.50)	0.62 (0.52 to 0.76)
Before Vacc.,Serotype 4 (n=189,183,186,198)	0.61 (0.52 to 0.72)	0.30 (0.25 to 0.37)	0.13 (0.11 to 0.16)	0.12 (0.10 to 0.15)
1M after Vacc.,Serotype 4 (n=190, 183, 186, 198)	2.59 (2.27 to 2.96)	8.37 (7.28 to 9.62)	9.76 (8.54 to 11.15)	6.37 (5.39 to 7.53)
Before Vacc.,Serotype 5 (n=189,183,186,198)	0.43 (0.36 to 0.50)	0.18 (0.15 to 0.22)	0.07 (0.06 to 0.08)	0.04 (0.03 to 0.06)
1M after Vacc.,Serotype 5 (n=190,183,186,198)	1.53 (1.32 to 1.77)	5.09 (4.32 to 5.99)	7.50 (6.52 to 8.63)	2.58 (1.88 to 3.53)
Before Vacc.,Serotype 6A (n=188,183,184,195)	1.61 (1.38 to 1.88)	0.71 (0.58 to 0.88)	0.50 (0.39 to 0.65)	0.28 (0.22 to 0.37)
1M after Vacc.,Serotype 6A (n=190,183,186,198)	7.59 (6.67 to 8.63)	31.99 (27.85 to 36.75)	46.28 (39.90 to 53.67)	20.03 (15.39 to 26.07)
Before Vacc.,Serotype 6B (n=188,183,182,195)	0.85 (0.71 to 1.02)	0.52 (0.42 to 0.63)	0.26 (0.20 to 0.32)	0.40 (0.31 to 0.51)
1M after Vacc.,Serotype 6B (n=190,183,186,198)	4.27 (3.69 to 4.94)	17.78 (15.43 to 20.48)	32.45 (27.90 to 37.74)	38.82 (31.49 to 47.86)
Before Vacc.,Serotype 7F (n=189,183,186,198)	1.17 (1.03 to 1.33)	0.51 (0.44 to 0.60)	0.18 (0.16 to 0.21)	0.11 (0.08 to 0.14)
1M after Vacc.,Serotype 7F (n=190,183,186,198)	3.53 (3.16 to 3.94)	6.42 (5.69 to 7.24)	7.92 (7.03 to 8.93)	3.19 (2.65 to 3.85)
Before Vacc.,Serotype 9V (n=189,183,186,198)	0.71 (0.61 to 0.83)	0.35 (0.28 to 0.42)	0.14 (0.11 to 0.17)	0.14 (0.11 to 0.18)
1M after Vacc.,Serotype 9V (n=190,183,186,198)	2.70 (2.35 to 3.09)	7.94 (6.83 to 9.24)	10.86 (9.41 to 12.54)	7.67 (6.52 to 9.02)
Before Vacc.,Serotype 14 (n=188,183,186,198)	1.53 (1.31 to 1.79)	0.66 (0.53 to 0.81)	0.42 (0.33 to 0.53)	0.29 (0.23 to 0.37)
1M after Vacc.,Serotype 14 (n=189,183,186,198)	4.42 (3.82 to 5.12)	14.60 (12.44 to 17.13)	28.54 (24.77 to 32.89)	28.17 (23.90 to 33.21)
Before Vacc.,Serotype 18C (n=189,183,186,198)	0.65 (0.55 to 0.76)	0.26 (0.21 to 0.32)	0.12 (0.09 to 0.14)	0.13 (0.11 to 0.17)
1M after Vacc.,Serotype 18C (n=190,183,186,198)	2.69 (2.32 to 3.12)	7.07 (6.01 to 8.32)	10.83 (9.53 to 12.30)	8.61 (7.34 to 10.10)
Before Vacc.,Serotype 19A (n=189,183,186,198)	0.47 (0.38 to 0.58)	0.52 (0.40 to 0.68)	0.78 (0.58 to 1.04)	0.55 (0.43 to 0.70)
1M after Vacc.,Serotype 19A (n=189,183,186,197)	3.29 (2.89 to 3.76)	12.48 (10.76 to 14.48)	13.65 (11.96 to 15.59)	8.89 (7.29 to 10.84)
Before Vacc.,Serotype 19F (n=189,183,186,198)	0.80 (0.67 to 0.94)	0.56 (0.44 to 0.71)	0.96 (0.70 to 1.32)	0.82 (0.63 to 1.06)
1M after Vacc.,Serotype 19F (n=190,183,186,198)	4.16 (3.61 to 4.79)	12.50 (10.48 to 14.91)	14.62 (12.32 to 17.36)	6.55 (5.60 to 7.66)

Before Vacc.,Serotype 23F (n=189,183,186,198)	0.96 (0.79 to 1.18)	0.90 (0.71 to 1.15)	0.82 (0.64 to 1.06)	0.61 (0.48 to 0.78)
1M after Vacc.,Serotype 23F (n=190,183,186,198)	5.35 (4.55 to 6.30)	16.18 (13.75 to 19.04)	22.69 (19.40 to 26.53)	19.16 (16.31 to 22.51)
Before Vacc.,Serotype 8 (n=186,179,185,196)	0.04 (0.03 to 0.05)	0.05 (0.04 to 0.06)	0.08 (0.07 to 0.10)	0.16 (0.12 to 0.20)
1M after Vacc.,Serotype 8 (n=190,182,186,198)	4.66 (4.17 to 5.22)	5.08 (4.45 to 5.80)	4.65 (4.05 to 5.34)	4.26 (3.67 to 4.94)
Before Vacc.,Serotype 10A (n=188,183,186,198)	0.01 (0.01 to 0.02)	0.03 (0.02 to 0.03)	0.07 (0.06 to 0.09)	0.15 (0.12 to 0.19)
1M after Vacc.,Serotype 10A (n=190,181,186,198)	1.23 (1.02 to 1.48)	2.76 (2.28 to 3.34)	3.98 (3.25 to 4.88)	5.35 (4.20 to 6.81)
Before Vacc.,Serotype 11A (n=188,183,186,198)	0.03 (0.02 to 0.03)	0.06 (0.04 to 0.08)	0.12 (0.09 to 0.16)	0.30 (0.23 to 0.38)
1M after Vacc.,Serotype 11A (n=190,182,186,198)	1.61 (1.40 to 1.86)	2.64 (2.25 to 3.09)	2.80 (2.35 to 3.33)	3.13 (2.60 to 3.77)
Before Vacc.,Serotype 12F (n=188,183,186,198)	0.01 (0.01 to 0.01)	0.01 (0.01 to 0.01)	0.01 (0.01 to 0.01)	0.01 (0.01 to 0.01)
1M after Vacc.,Serotype 12F (n=190,182,186,198)	0.22 (0.18 to 0.27)	0.38 (0.31 to 0.46)	0.36 (0.29 to 0.44)	0.28 (0.22 to 0.34)
Before Vacc.,Serotype 15B (n=188,182,186,198)	0.02 (0.02 to 0.03)	0.05 (0.04 to 0.07)	0.20 (0.15 to 0.27)	0.35 (0.27 to 0.45)
1M after Vacc.,Serotype 15B (n=190,181,186,198)	1.17 (0.97 to 1.40)	3.96 (3.12 to 5.03)	10.74 (8.49 to 13.60)	18.79 (15.16 to 23.28)
Before Vacc.,Serotype 22F (n=188,183,186,198)	0.01 (0.00 to 0.01)	0.02 (0.01 to 0.02)	0.08 (0.06 to 0.11)	0.14 (0.11 to 0.19)
1M after Vacc.,Serotype 22F (n=190,182,186,198)	9.57 (8.12 to 11.29)	12.46 (10.82 to 14.35)	15.68 (13.45 to 18.29)	12.36 (10.38 to 14.72)
Before Vacc.,Serotype 33F (n=188,183,185,196)	0.02 (0.01 to 0.02)	0.04 (0.03 to 0.05)	0.10 (0.08 to 0.12)	0.18 (0.14 to 0.22)
1M after Vacc.,Serotype 33F (n=190,182,185,197)	1.91 (1.60 to 2.27)	3.16 (2.63 to 3.79)	3.87 (3.24 to 4.61)	3.93 (3.25 to 4.75)

Statistical analyses

No statistical analyses for this end point

Secondary: GMFRs of Pneumococcal Serotype-Specific IgG Concentrations for the 13vPnC Serotypes From Before to 1 Month After Vaccination: Cohort 1 and 2

End point title	GMFRs of Pneumococcal Serotype-Specific IgG Concentrations for the 13vPnC Serotypes From Before to 1 Month After Vaccination: Cohort 1 and 2[14]

End point description:

Pneumococcal serotype-specific IgG concentrations were measured from serum samples for 13vPnC serotypes: 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F and 23F. GMFR was calculated as geometric mean of fold rise from before vaccination on Day 1 to 1 month after vaccination with 20vPnC. GMFRs and the corresponding 2-sided CIs were calculated by exponentiating the mean logarithm of the titres or fold rises and the corresponding CIs (based on the Student t distribution). EIP included all subjects who were eligible; received 20vPnC; at least 1 valid immunogenicity result from 1 month after vaccination collected within 27 to 56 days after vaccination for Cohorts 1-2; no other major protocol deviations. Here, "Number of Subjects Analysed" signifies subjects included in the EIP and n=subjects with valid assay results at both timepoints for the specified serotype.

End point type	Secondary

End point timeframe:

Before vaccination to 1 month after vaccination

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint was planned to be analysed only for the specified reporting arms.

End point values	Cohort 1: 20vPnC: >=15 to <24 Months	Cohort 2: 20vPnC: >=2 to <5 Years		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	190	183		
Units: Fold-rise				
geometric mean (confidence interval 95%)				
Serotype 1 (n=189, 183)	3.4 (3.0 to 3.9)	20.6 (17.2 to 24.7)		
Serotype 3 (n=189, 183)	3.9 (3.4 to 4.5)	14.9 (12.4 to 17.9)		
Serotype 4 (n=189, 183)	4.3 (3.7 to 5.0)	27.6 (22.7 to 33.5)		
Serotype 5 (n=189, 183)	3.6 (3.1 to 4.2)	28.2 (23.0 to 34.6)		
Serotype 6A (n=188, 183)	4.8 (4.1 to 5.6)	44.9 (35.8 to 56.3)		
Serotype 6B (n=188, 183)	5.0 (4.3 to 5.9)	34.5 (28.3 to 42.0)		
Serotype 7F (n=189, 183)	3.0 (2.7 to 3.4)	12.5 (10.5 to 14.9)		
Serotype 9V (n=189, 183)	3.8 (3.3 to 4.4)	23.0 (19.0 to 27.8)		
Serotype 14 (n=187, 183)	2.9 (2.5 to 3.3)	22.2 (18.0 to 27.4)		
Serotype 18C (n=189, 183)	4.2 (3.6 to 4.9)	27.2 (22.5 to 32.9)		
Serotype 19A (n=188, 183)	6.9 (5.7 to 8.4)	24.1 (19.0 to 30.6)		
Serotype 19F (n=189, 183)	5.2 (4.4 to 6.3)	22.3 (17.2 to 28.8)		
Serotype 23F (n=189, 183)	5.6 (4.8 to 6.6)	17.9 (14.6 to 21.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: GMFRs of Pneumococcal Serotype-Specific IgG Concentrations for the 20vPnC Serotypes From Before to 1 Month After Vaccination: Cohort 3 and 4

End point title	GMFRs of Pneumococcal Serotype-Specific IgG Concentrations for the 20vPnC Serotypes From Before to 1 Month After Vaccination: Cohort 3 and 4[15]

End point description:

Pneumococcal serotype-specific IgG concentrations were measured from serum samples for 13vPnC serotypes: 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F and 23F; and 7 additional 20vPnC serotypes: 8, 10A, 11A, 12F, 15B, 22F and 33F. GMFR was calculated as geometric mean of fold rise from before vaccination on Day 1 to 1 month after vaccination with 20vPnC. GMFRs and the corresponding 2-sided CIs were calculated by exponentiating the mean logarithm of the titres or fold rises and the corresponding CIs (based on the Student t distribution). EIP included all subjects who were eligible;

received 20vPnC; at least 1 valid immunogenicity result from 1 month after vaccination collected within 27 to 49 days after vaccination for Cohorts 3-4; no other major protocol deviations. Here, "Number of Subjects Analysed" signifies subjects included in the EIP and n= subjects with valid assay results at both timepoints for the specified serotype.

End point type	Secondary

End point timeframe:

Before vaccination to 1 month after vaccination

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint was planned to be analysed only for the specified reporting arms.

End point values	Cohort 3: 20vPnC: >=5 to <10 Years	Cohort 4: 20vPnC: >=10 to <18 Years		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	186	198		
Units: Fold-rise				
geometric mean (confidence interval 95%)				
Serotype: 1 (n=186, 198)	49.4 (41.6 to 58.6)	44.2 (37.0 to 52.9)		
Serotype: 3 (n=186, 198)	5.9 (4.6 to 7.5)	4.3 (3.5 to 5.2)		
Serotype: 4 (n=186, 198)	74.1 (61.4 to 89.4)	52.0 (42.3 to 64.0)		
Serotype: 5 (n=186, 198)	107.0 (89.4 to 128.2)	59.3 (47.6 to 73.9)		
Serotype: 6A (n=184, 195)	91.9 (67.7 to 124.9)	72.5 (54.9 to 95.7)		
Serotype: 6B (n=182, 195)	127.9 (101.0 to 162.0)	99.5 (77.1 to 128.3)		
Serotype: 7F (n=186, 198)	42.9 (36.1 to 51.1)	30.0 (24.0 to 37.6)		
Serotype: 9V (n=186, 198)	80.3 (64.3 to 100.3)	54.2 (42.7 to 68.9)		
Serotype: 14 (n=186, 198)	68.4 (53.4 to 87.7)	96.7 (76.6 to 122.1)		
Serotype: 18C (n=186, 198)	93.7 (76.9 to 114.1)	64.5 (52.3 to 79.4)		
Serotype: 19A (n=186, 197)	17.6 (13.2 to 23.4)	16.2 (13.1 to 20.0)		
Serotype: 19F (n=186, 198)	15.2 (10.5 to 22.0)	8.0 (6.0 to 10.7)		
Serotype: 23F (n=186, 198)	27.6 (21.0 to 36.3)	31.4 (23.8 to 41.5)		
Serotype: 8 (n=185, 196)	55.2 (44.8 to 67.9)	27.3 (21.9 to 33.9)		
Serotype: 10A (n=186, 198)	54.8 (44.4 to 67.7)	35.9 (29.3 to 43.9)		
Serotype: 11A (n=186, 198)	23.6 (18.6 to 29.9)	10.5 (8.5 to 12.9)		
Serotype: 12F (n=186, 198)	31.9 (26.7 to 38.3)	21.4 (17.6 to 26.0)		
Serotype: 15B (n=186, 198)	52.6 (41.3 to 66.9)	53.8 (43.1 to 67.1)		
Serotype: 22F (n=186, 198)	187.7 (134.6 to 261.7)	86.2 (64.9 to 114.4)		
Serotype: 33F (n=184, 195)	39.3 (31.6 to 49.0)	22.4 (18.2 to 27.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With >=4-fold Rise in Pneumococcal Serotype-Specific OPA Titres for the 7 Additional Serotypes From Before to 1 Month After Vaccination: Cohorts 2, 3, and 4 Only

End point title	Percentage of Subjects With >=4-fold Rise in Pneumococcal Serotype-Specific OPA Titres for the 7 Additional Serotypes From Before to 1 Month After Vaccination: Cohorts 2, 3, and 4 Only[16]

End point description:

Pneumococcal serotype-specific OPA titres were measured from serum samples for 7 additional 20vPnC serotypes: 8, 10A, 11A, 12F, 15B, 22F and 33F. Percentage of subjects with >=4 fold rise in serotype-specific OPA titres from before vaccination to 1 month after vaccination with 20vPnC and the associated 2-sided 95% CI based on the Clopper and Pearson method was presented. EIP included all subjects who were eligible; received 20vPnC; at least 1 valid immunogenicity result from 1 month after vaccination collected within 27 to 56 days or 27 to 49 days after vaccination for Cohort 2 or Cohorts 3-4, respectively; no other major protocol deviations. Here, "Number of Subjects Analysed" signifies subjects included in the EIP and n=subjects with valid assay results at both timepoints for the specified serotype.

End point type	Secondary

End point timeframe:

Before vaccination to 1 month after vaccination

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analysed only for the specified reporting arms.

End point values	Cohort 2: 20vPnC: >=2 to <5 Years	Cohort 3: 20vPnC: >=5 to <10 Years	Cohort 4: 20vPnC: >=10 to <18 Years	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	183	186	198	
Units: Percentage of subjects				
number (confidence interval 95%)				
Serotype: 8 (n=74, 153, 174)	93.2 (84.9 to 97.8)	92.2 (86.7 to 95.9)	89.1 (83.5 to 93.3)	
Serotype: 10A (n=73, 134, 142)	84.9 (74.6 to 92.2)	80.6 (72.9 to 86.9)	81.7 (74.3 to 87.7)	
Serotype: 11A (n=52, 136, 155)	86.5 (74.2 to 94.4)	66.2 (57.6 to 74.1)	62.6 (54.5 to 70.2)	
Serotype: 12F (n=74, 154, 164)	94.6 (86.7 to 98.5)	96.8 (92.6 to 98.9)	94.5 (89.8 to 97.5)	
Serotype: 15B (n=76, 142, 164)	88.2 (78.7 to 94.4)	89.4 (83.2 to 94.0)	93.9 (89.1 to 97.0)	
Serotype: 22F (n=68, 137, 168)	86.8 (76.4 to 93.8)	87.6 (80.9 to 92.6)	81.0 (74.2 to 86.6)	
Serotype: 33F (n=73, 144, 158)	71.2 (59.4 to 81.2)	79.9 (72.4 to 86.1)	75.3 (67.8 to 81.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titers (GMTs) of Pneumococcal Serotype-Specific OPA Titers for the 20vPnC Serotypes Before and 1 Month After Vaccination

End point title	Geometric Mean Titers (GMTs) of Pneumococcal Serotype-Specific OPA Titers for the 20vPnC Serotypes Before and 1 Month After Vaccination

End point description:

Pneumococcal serotype-specific OPA titres were measured from serum samples for 13vPnC serotypes: 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F; and 7 additional 20vPnC serotypes: 8, 10A, 11A, 12F, 15B, 22F and 33F. GMTs and 2-sided CIs were calculated by exponentiating the mean logarithm of the titres and the corresponding CIs (based on the Student t distribution). EIP included all subjects who were eligible; received 20vPnC; at least 1 valid immunogenicity result from 1 month after vaccination collected within 27 to 56 days or 27 to 49 days after vaccination for Cohorts 1-2 or Cohorts 3-4,respectively; no other major protocol deviations. Here, "Number of Subjects Analysed" signifies subjects included in the EIP and n=subjects with valid OPA titres at the specified timepoint.

End point type	Secondary

End point timeframe:

Before vaccination (Vacc.) and 1 month after vaccination (1M after Vacc.)

End point values	Cohort 1: 20vPnC: >=15 to <24 Months	Cohort 2: 20vPnC: >=2 to <5 Years	Cohort 3: 20vPnC: >=5 to <10 Years	Cohort 4: 20vPnC: >=10 to <18 Years
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	190	183	186	198
Units: Titer				
geometric mean (confidence interval 95%)				
Before Vacc., Serotype 1 (n=46, 47, 93, 96)	14 (11 to 18)	12 (10 to 14)	10 (9 to 11)	11 (9 to 12)
1M after Vacc.Serotype 1 (n=44,46, 93, 96)	57 (39 to 84)	360 (272 to 476)	548 (455 to 660)	396 (302 to 519)
Before Vacc., Serotype 3 (n=46, 47, 94, 95)	21 (15 to 29)	15 (11 to 22)	29 (22 to 40)	19 (14 to 24)
1M after Vacc.Serotype 3 (n=44, 46, 92, 94)	80 (62 to 103)	150 (116 to 195)	155 (135 to 178)	105 (88 to 124)
Before Vacc., Serotype: 4 (n=41, 45, 82, 86)	42 (24 to 75)	34 (19 to 62)	43 (27 to 67)	34 (22 to 51)
1M after Vacc.Serotype 4 (n=43, 44, 88, 93)	563 (342 to 927)	1729 (1188 to 2516)	2328 (1942 to 2789)	2290 (1822 to 2878)
Before Vacc., Serotype: 5 (n=46,47, 94, 96)	18 (16 to 21)	17 (15 to 20)	15 (15 to 15)	15 (15 to 16)
1M after Vacc.Serotype 5, (n=44, 46, 92, 96)	51 (38 to 68)	198 (143 to 276)	385 (324 to 458)	216 (159 to 294)
Before Vacc., Serotype: 6A (n=46, 47, 90, 91)	137 (77 to 243)	96 (55 to 168)	74 (51 to 106)	64 (44 to 91)

1M after Vacc.Serotype 6A (n=43, 46, 92, 96)	1707 (1144 to 2547)	5283 (3954 to 7060)	8268 (6617 to 10331)	9434 (7616 to 11686)
Before Vacc., Serotype: 6B (n=44, 43, 78, 90)	110 (67 to 182)	126 (72 to 219)	156 (99 to 244)	237 (155 to 363)
1M after Vacc.Serotype 6B (n=44, 46, 90, 93)	943 (611 to 1455)	3273 (2390 to 4482)	6569 (5367 to 8040)	10085 (8263 to 12309)
Before Vacc., Serotype 7F (n=41, 45, 81, 86)	705 (492 to 1010)	996 (748 to 1327)	541 (410 to 713)	516 (381 to 698)
1M after Vacc.Serotype 7F (n=42, 44, 87, 93)	2635 (2105 to 3297)	3409 (2552 to 4556)	3981 (3446 to 4598)	3326 (2878 to 3843)
Before Vacc., Serotype: 9V (n=39, 45, 84, 92)	649 (350 to 1204)	323 (202 to 515)	410 (289 to 580)	469 (330 to 667)
1M after Vacc.Serotype 9V (n=43, 44, 87, 93)	7686 (5718 to 10332)	7210 (4781 to 10876)	11717 (9262 to 14823)	9627 (7492 to 12369)
Before Vacc., Serotype: 14 (n=46, 44, 90, 92)	242 (151 to 387)	300 (186 to 484)	246 (172 to 353)	97 (65 to 145)
1M after Vacc.Serotype 14 (n=44, 46, 93, 96)	1018 (748 to 1385)	2506 (1932 to 3249)	4610 (3688 to 5762)	3925 (3153 to 4885)
Before Vacc., Serotype: 18C (n=38, 44, 76, 87)	300 (147 to 613)	139 (69 to 277)	152 (89 to 261)	73 (45 to 119)
1M after Vacc.Serotype 18C (n=43, 44, 87, 93)	3749 (2740 to 5131)	5344 (3809 to 7498)	6766 (5585 to 8197)	3617 (2816 to 4645)
Before Vacc., Serotype: 19A (n=40, 47, 86, 90)	138 (71 to 271)	84 (45 to 156)	117 (76 to 181)	66 (44 to 100)
1M after Vacc.Serotype: 19A (n=43, 44, 88, 93)	1708 (1192 to 2448)	2640 (1943 to 3587)	2162 (1786 to 2618)	2212 (1801 to 2717)
Before Vacc., Serotype: 19F (n=45, 47, 94, 93)	44 (31 to 61)	44 (31 to 61)	91 (66 to 125)	57 (44 to 73)
1M after Vacc.Serotype 19F (n=44, 46, 92, 96)	267 (169 to 421)	928 (618 to 1394)	1095 (810 to 1479)	551 (401 to 757)
Before Vacc., Serotype 23F (n=41, 46, 87, 92)	139 (67 to 288)	206 (108 to 394)	87 (53 to 145)	46 (29 to 73)
1M after Vacc.Serotype 23F (n=43, 44, 88, 93)	1936 (1385 to 2707)	2493 (1757 to 3539)	2213 (1751 to 2797)	1842 (1391 to 2439)
Before Vacc., Serotype: 8 (n=86, 82, 164, 185)	30 (24 to 39)	39 (29 to 54)	34 (28 to 42)	35 (28 to 43)
1M after Vacc.Serotyp 8 (n=85, 80, 175, 187)	4758 (3763 to 6016)	4428 (3467 to 5654)	3870 (3302 to 4535)	3125 (2680 to 3642)
Before Vacc., Serotype: 10A (n=84, 82, 158, 168)	92 (60 to 141)	275 (160 to 472)	745 (519 to 1071)	554 (395 to 777)
1M after Vacc.Serotype 10A (n=86, 78, 159, 171)	10626 (7825 to 14429)	14345 (10473 to 19649)	21102 (17238 to 25833)	17417 (14301 to 21214)
Before Vacc., Serotype 11A (n=68, 60, 147, 165)	88 (60 to 127)	436 (237 to 800)	1347 (962 to 1887)	765 (543 to 1076)
1M after Vacc.Serotype: 11A (n=84, 78, 172, 186)	13350 (10540 to 16910)	14093 (9904 to 20054)	16882 (13650 to 20880)	11677 (9751 to 13982)
Serotype: 12F (n=92, 86, 174, 182)	38 (29 to 50)	37 (27 to 50)	48 (38 to 60)	46 (36 to 59)
1M after Vacc.Serotype: 12F (n=84, 76, 164, 180)	16924 (13400 to 21376)	13257 (9463 to 18572)	23860 (19002 to 29959)	20250 (16861 to 24320)
Before Vacc., Serotype: 15B (n=94, 84, 163, 187)	30 (21 to 45)	111 (63 to 197)	79 (54 to 115)	45 (33 to 61)
1M after Vacc.Serotype: 15B (n=86, 80, 163, 174)	22951 (17380 to 30307)	27095 (19557 to 37538)	25729 (19647 to 33695)	21496 (16697 to 27672)
Before Vacc., Serotype: 22F (n=87, 80, 161, 184)	21 (13 to 33)	104 (55 to 194)	259 (170 to 394)	243 (161 to 366)
1M after Vacc.Serotype 22F (n=81, 74, 158, 179)	22464 (16840 to 29967)	25573 (18096 to 36141)	33615 (26198 to 43130)	27922 (22622 to 34463)
Before Vacc., Serotype: 33F (n=91, 85, 170, 177)	1154 (861 to 1548)	2179 (1694 to 2804)	3334 (2847 to 3905)	2895 (2448 to 3424)
1M after Vacc.Serotype 33F (n=81, 76, 155, 171)	23431 (17375 to 31598)	28076 (19255 to 40938)	45921 (36768 to 57353)	32363 (26219 to 39946)

Statistical analyses

No statistical analyses for this end point

Secondary: GMFRs of Pneumococcal Serotype-Specific OPA Titres for the 20vPnC Serotypes From Before to 1 Month After Vaccination: Cohorts 1 and 2

End point title	GMFRs of Pneumococcal Serotype-Specific OPA Titres for the 20vPnC Serotypes From Before to 1 Month After Vaccination: Cohorts 1 and 2[17]

End point description:

Pneumococcal serotype-specific OPA titres were measured from serum samples for 13vPnC serotypes: 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F; and 7 additional 20vPnC serotypes: 8, 10A, 11A, 12F, 15B, 22F and 33F. GMFR was calculated as geometric mean of fold rise from before vaccination on Day 1 to 1 month after vaccination with 20vPnC. GMFRs and the corresponding 2-sided CIs were calculated by exponentiating the mean logarithm of the titres or fold rises and the corresponding CIs (based on the Student t distribution). EIP included all subjects who were eligible; received 20vPnC; at least 1 valid immunogenicity result from 1 month after vaccination collected within 27 to 56 days after vaccination for Cohorts 1-2; no other major protocol deviations. Here, 'Number of Subjects Analysed' signifies subjects included in the EIP and n=subjects with valid assay results at both timepoints for the specified serotype.

End point type	Secondary

End point timeframe:

Before vaccination to 1 month after vaccination

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint was planned to be analysed only for the specified reporting arms.

End point values	Cohort 1: 20vPnC: >=15 to <24 Months	Cohort 2: 20vPnC: >=2 to <5 Years		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	190	183		
Units: Fold rise				
geometric mean (confidence interval 95%)				
Serotype 1 (n=42, 46)	4.1 (2.9 to 6.0)	29.8 (21.2 to 41.9)		
Serotype 3 (n=42, 46)	3.7 (2.6 to 5.3)	9.6 (7.1 to 13.1)		
Serotype 4 (n=40, 41)	13.2 (7.0 to 25.0)	50.0 (26.7 to 93.6)		
Serotype 5 (n=42, 46)	2.8 (2.0 to 3.8)	11.4 (8.2 to 16.0)		
Serotype 6A (n=41, 46)	12.7 (8.1 to 20.0)	52.9 (30.8 to 90.9)		
Serotype 6B (n=40, 42)	7.8 (4.6 to 13.2)	24.4 (14.4 to 41.2)		
Serotype 7F (n=39, 41)	3.6 (2.5 to 5.2)	3.6 (2.7 to 4.8)		
Serotype 9V (n=38, 42)	11.5 (6.2 to 21.3)	23.1 (14.7 to 36.5)		

Serotype 14 (n=42, 43)	3.9 (2.5 to 6.1)	8.3 (5.1 to 13.4)		
Serotype 18C (n=38, 40)	12.7 (6.6 to 24.5)	40.6 (20.7 to 79.6)		
Serotype 19A (n=39, 43)	11.1 (6.2 to 19.8)	33.5 (17.3 to 65.0)		
Serotype 19F (n=41, 46)	5.7 (3.3 to 9.7)	21.0 (13.0 to 33.9)		
Serotype 23F (n=40, 42)	12.5 (6.7 to 23.6)	10.7 (6.2 to 18.5)		
Serotype 8 (n=76, 74)	155.9 (110.4 to 220.2)	105.4 (67.6 to 164.3)		
Serotype 10A (n=76, 73)	121.7 (74.7 to 198.4)	53.3 (28.7 to 99.0)		
Serotype 11A (n=60, 52)	161.4 (115.7 to 225.2)	34.7 (17.1 to 70.4)		
Serotype 12F (n=81, 74)	437.2 (307.0 to 622.7)	319.9 (193.9 to 527.9)		
Serotype 15B (n=84, 76)	717.6 (449.8 to 1144.6)	294.4 (149.1 to 581.3)		
Serotype 22F (n=74, 68)	983.6 (580.9 to 1665.5)	224.6 (104.9 to 480.9)		
Serotype 33F (n=78, 73)	18.8 (13.1 to 27.2)	12.4 (7.4 to 20.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: GMFRs of Pneumococcal Serotype-Specific OPA Titres for the 13vPnC Serotypes From Before to 1 Month After Vaccination: Cohorts 3 and 4

End point title	GMFRs of Pneumococcal Serotype-Specific OPA Titres for the 13vPnC Serotypes From Before to 1 Month After Vaccination: Cohorts 3 and 4[18]

End point description:

Pneumococcal serotype-specific OPA titres were measured for 13vPnC serotypes: 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F. GMFR was calculated as geometric mean of fold rise from before vaccination on Day 1 to 1 month after vaccination with 20vPnC. GMFRs and the corresponding 2-sided CIs were calculated by exponentiating the mean logarithm of the titres or fold rises and the corresponding CIs (based on the Student t distribution). EIP included all subjects who were eligible; received 20vPnC; at least 1 valid immunogenicity result from 1 month after vaccination collected within 27 to 49 days after vaccination for Cohorts 3-4; no other major protocol deviations. Here, "Number of Subjects Analysed" signifies subjects included in the EIP and n=subjects with valid assay results at both timepoints for the specified serotype.

End point type	Secondary

End point timeframe:

Before vaccination to 1 month after vaccination

Notes:

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analysed only for the specified reporting arms.

End point values	Cohort 3: 20vPnC: >=5 to <10 Years	Cohort 4: 20vPnC: >=10 to <18 Years		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	186	198		
Units: Fold rise				
geometric mean (confidence interval 95%)				
Serotype 1 (n=91, 96)	55.2 (45.1 to 67.4)	37.3 (28.7 to 48.6)		
Serotype 3 (n=91, 93)	5.3 (3.9 to 7.2)	5.8 (4.5 to 7.5)		
Serotype 4 (n=80, 86)	50.2 (31.6 to 79.5)	65.6 (41.4 to 103.7)		
Serotype 5 (n=91, 96)	26.7 (22.4 to 31.8)	14.4 (10.5 to 19.6)		
Serotype 6A (n=87, 91)	110.3 (68.7 to 177.1)	147.9 (96.0 to 228.0)		
Serotype 6B (n=73, 87)	38.8 (22.7 to 66.3)	42.0 (26.1 to 67.6)		
Serotype 7F (n=78, 86)	7.0 (5.3 to 9.3)	6.2 (4.4 to 8.8)		
Serotype 9V (n=82, 92)	28.9 (19.7 to 42.5)	20.4 (13.4 to 31.0)		
Serotype 14 (n=88, 92)	18.1 (12.2 to 26.8)	38.9 (25.1 to 60.3)		
Serotype 18C (n=74, 87)	46.2 (26.8 to 79.6)	47.3 (28.7 to 78.0)		
Serotype 19A (n=84, 90)	17.5 (10.8 to 28.3)	33.1 (20.7 to 53.1)		
Serotype 19F (n=91, 93)	11.7 (7.4 to 18.5)	10.0 (6.7 to 15.0)		
Serotype 23F (n=85, 92)	26.9 (16.3 to 44.5)	39.4 (23.7 to 65.7)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Local reactions and systemic events (systematic assessment): within 7 days after vaccination; SAEs (non-systematic assessment): from Day1 up to 6 months after vaccination and other AEs (non-systematic assessment): from Day1 up to 1 month after vaccination

Adverse event reporting additional description:

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

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups

Reporting group title	Cohort 1: 20vPnC: >=15 to <24 Months

Reporting group description:

Subjects aged >=15 months to <24 months who have been previously vaccinated with at least 3 doses of 13vPnC, were administered a single dose of 0.5 mL 20vPnC intramuscularly on Day 1.

Reporting group title	Cohort 2: 20vPnC: >=2 to <5 Years

Reporting group description:

Subjects aged >=2 to <5 years who have been previously vaccinated with at least 3 doses of 13vPnC, were administered a single dose of 0.5 mL 20vPnC intramuscularly on Day 1.

Reporting group title	Cohort 3: 20vPnC: >=5 to <10 Years

Reporting group description:

Subjects aged >=5 to <10 years regardless of previous vaccination status with 7vPnC or 13vPnC, were administered a single dose of 0.5 mL 20vPnC intramuscularly into the left arm on Day 1.

Reporting group title	Cohort 4: 20vPnC: >=10 to <18 Years

Reporting group description:

Subjects aged >=10 to <18 years regardless of previous vaccination status with 7vPnC or 13vPnC, were administered a single dose of 0.5 mL 20vPnC intramuscularly into the left arm on Day 1.

Serious adverse events	Cohort 1: 20vPnC: >=15 to <24 Months	Cohort 2: 20vPnC: >=2 to <5 Years	Cohort 3: 20vPnC: >=5 to <10 Years
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 209 (0.96%)	0 / 216 (0.00%)	0 / 201 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Papillary thyroid cancer			
subjects affected / exposed	0 / 209 (0.00%)	0 / 216 (0.00%)	0 / 201 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			

Near drowning			
subjects affected / exposed	1 / 209 (0.48%)	0 / 216 (0.00%)	0 / 201 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 209 (0.00%)	0 / 216 (0.00%)	0 / 201 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile convulsion			
subjects affected / exposed	1 / 209 (0.48%)	0 / 216 (0.00%)	0 / 201 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 209 (0.00%)	0 / 216 (0.00%)	0 / 201 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Cohort 4: 20vPnC: >=10 to <18 Years		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 205 (1.46%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Papillary thyroid cancer			
subjects affected / exposed	1 / 205 (0.49%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Near drowning			
subjects affected / exposed	0 / 205 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			

Headache			
subjects affected / exposed	1 / 205 (0.49%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Febrile convulsion			
subjects affected / exposed	0 / 205 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 205 (0.49%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Cohort 1: 20vPnC: >=15 to <24 Months	Cohort 2: 20vPnC: >=2 to <5 Years	Cohort 3: 20vPnC: >=5 to <10 Years
Total subjects affected by non-serious adverse events			
subjects affected / exposed	173 / 209 (82.78%)	163 / 216 (75.46%)	178 / 201 (88.56%)
Nervous system disorders			
Headache (HEADACHE)			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 209 (0.00%)	12 / 216 (5.56%)	37 / 201 (18.41%)
occurrences (all)	0	13	45
Hypersomnia (INCREASED SLEEP)			
alternative assessment type: Systematic			
subjects affected / exposed	85 / 209 (40.67%)	0 / 216 (0.00%)	0 / 201 (0.00%)
occurrences (all)	104	0	0
General disorders and administration site conditions			
Injection site erythema (REDNESS)			
alternative assessment type: Systematic			
subjects affected / exposed	77 / 209 (36.84%)	84 / 216 (38.89%)	74 / 201 (36.82%)
occurrences (all)	84	86	79
Injection site pain (PAIN)			

alternative assessment type: Systematic			
subjects affected / exposed	107 / 209 (51.20%)	142 / 216 (65.74%)	165 / 201 (82.09%)
occurrences (all)	115	157	178
Injection site swelling (SWELLING)			
alternative assessment type: Systematic			
subjects affected / exposed	45 / 209 (21.53%)	50 / 216 (23.15%)	54 / 201 (26.87%)
occurrences (all)	51	54	57
Pyrexia (FEVER)			
alternative assessment type: Systematic			
subjects affected / exposed	24 / 209 (11.48%)	7 / 216 (3.24%)	1 / 201 (0.50%)
occurrences (all)	25	9	1
Fatigue (FATIGUE)			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 209 (0.00%)	80 / 216 (37.04%)	56 / 201 (27.86%)
occurrences (all)	0	98	76
Psychiatric disorders			
Irritability (IRRITABILITY)			
alternative assessment type: Systematic			
subjects affected / exposed	126 / 209 (60.29%)	0 / 216 (0.00%)	0 / 201 (0.00%)
occurrences (all)	170	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia (JOINT PAIN)			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 209 (0.00%)	8 / 216 (3.70%)	13 / 201 (6.47%)
occurrences (all)	0	9	14
Myalgia (MUSCLE PAIN)			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 209 (0.00%)	57 / 216 (26.39%)	78 / 201 (38.81%)
occurrences (all)	0	63	86
Metabolism and nutrition disorders			
Decreased appetite (DECREASED APPETITE)			
alternative assessment type: Systematic			
subjects affected / exposed	51 / 209 (24.40%)	0 / 216 (0.00%)	0 / 201 (0.00%)
occurrences (all)	72	0	0

Non-serious adverse events	Cohort 4: 20vPnC: >=10 to <18 Years		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	186 / 205 (90.73%)		
Nervous system disorders			
Headache (HEADACHE)			
alternative assessment type: Systematic			
subjects affected / exposed	60 / 205 (29.27%)		
occurrences (all)	75		
Hypersomnia (INCREASED SLEEP)			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 205 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Injection site erythema (REDNESS)			
alternative assessment type: Systematic			
subjects affected / exposed	31 / 205 (15.12%)		
occurrences (all)	32		
Injection site pain (PAIN)			
alternative assessment type: Systematic			
subjects affected / exposed	168 / 205 (81.95%)		
occurrences (all)	175		
Injection site swelling (SWELLING)			
alternative assessment type: Systematic			
subjects affected / exposed	32 / 205 (15.61%)		
occurrences (all)	34		
Pyrexia (FEVER)			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 205 (0.00%)		
occurrences (all)	0		
Fatigue (FATIGUE)			
alternative assessment type: Systematic			
subjects affected / exposed	57 / 205 (27.80%)		
occurrences (all)	66		
Psychiatric disorders			

Irritability (IRRITABILITY) alternative assessment type: Systematic subjects affected / exposed occurrences (all)	 0 / 205 (0.00%) 0		
Musculoskeletal and connective tissue disorders Arthralgia (JOINT PAIN) alternative assessment type: Systematic subjects affected / exposed occurrences (all) Myalgia (MUSCLE PAIN) alternative assessment type: Systematic subjects affected / exposed occurrences (all)	 17 / 205 (8.29%) 17 99 / 205 (48.29%) 108		
Metabolism and nutrition disorders Decreased appetite (DECREASED APPETITE) alternative assessment type: Systematic subjects affected / exposed occurrences (all)	 0 / 205 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 October 2021	-To be consistent with the European PIP modification approved in August 2021 added 2 secondary immunogenicity endpoints. -Added 2 exploratory immunogenicity endpoints for additional description of the immune response. - Clarified that the primary immunogenicity endpoints and the additional secondary endpoints are addressing consistencies with the approved European PIP modification.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported