



Clinical trial results:

A PHASE 3, RANDOMIZED, PARTIALLY DOUBLE-BLIND TRIAL TO EVALUATE THE SAFETY AND IMMUNOGENICITY OF 20-VALENT PNEUMOCOCCAL CONJUGATE VACCINE (20-vPnC) IN HEALTHY TODDLERS 12 THROUGH 23 MONTHS OF AGE WITH 2 PRIOR INFANT DOSES OF PREVENAR 13

Summary

EudraCT number	2021-006624-41
Trial protocol	HU ES PL
Global end of trial date	01 June 2023

Results information

Result version number	v1 (current)
This version publication date	14 December 2023
First version publication date	14 December 2023

Trial information

Trial identification

Sponsor protocol code	B7471027
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05408429
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer Inc.
Sponsor organisation address	66 Hudson Boulevard East, New York, United States, NY 10001
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)	EMA-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	21 August 2023
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	01 June 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To describe the safety and immunogenicity of 1 or 2 doses of 20vPnC in toddlers greater than or equal to ($\geq$) 12 to less than ($<$) 24 months of age who have received 2 doses of 13vPnC in infancy (prior to 12 months of age).

Safety assessments included local reactions, systemic events and adverse events. Immunogenicity assessments included percentage of subjects with pre-defined IG concentrations, IgG GMCs and OPA GMTs 1 month after the last vaccination.

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 on 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	24 June 2022
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	Hungary: 124
Country: Number of subjects enrolled	Poland: 70
Country: Number of subjects enrolled	Spain: 162
Worldwide total number of subjects	356
EEA total number of subjects	356

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)	356
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:

Subjects included in this study were toddlers ≥ 12 to less than < 24 months of age who had received 2 doses of 13vPnC (Prevenar 13®) in infancy (prior to 12 months of age).

Pre-assignment

Screening details:

356 subjects were enrolled and randomized to receive either 2 dose of 20vPnC, 1 dose of 20vPnC or 1 dose of 13vPnC.

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	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	2-Dose 20vPnC

Arm description:

Toddlers ≥ 12 to < 24 months of age were randomised to receive 2 doses of 0.5 milliliter (mL) 20vPnC intramuscularly. Dose 1 was administered at Day 1 (Dose 1 Visit) and Dose 2 was administered 56 to 70 days later (Dose 2 Visit).

Arm type	Experimental
Investigational medicinal product name	20vPnC
Investigational medicinal product code	PF-06482077
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 0.5 mL dose of 20vPnC intramuscularly each on Day 1 (Dose 1 Visit 1) and 56 to 70 days later (Dose 2 Visit).

Arm title	1-Dose 20vPnC
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Arm description:

Toddlers ≥ 12 to < 24 months of age were randomised to receive 1 dose of 0.5 mL 20vPnC intramuscularly on Day 1 (Dose 1 Visit).

Arm type	Experimental
Investigational medicinal product name	20vPnC
Investigational medicinal product code	PF-06482077
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 0.5 mL dose of 20vPnC intramuscularly each on Day 1 (Dose 1 Visit 1).

Arm title	13vPnC Control
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Arm description:

Toddlers ≥ 12 to < 24 months of age were randomised to receive 1 dose of 0.5 mL 13vPnC intramuscularly on Day 1 (Dose 1 Visit).

Arm type	Active comparator
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Investigational medicinal product name	13-Valent Pneumococcal Conjugate Vaccine
Investigational medicinal product code	
Other name	Prevenar 13®
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 0.5 mL dose of 13vPnC intramuscularly each on Day 1 (Dose 1 Visit 1).

Number of subjects in period 1	2-Dose 20vPnC	1-Dose 20vPnC	13vPnC Control
Started	121	118	117
Completed	115	117	116
Not completed	6	1	1
Consent withdrawn by subject	5	-	1
Lost to follow-up	1	1	-

Baseline characteristics

Reporting groups

Reporting group title	2-Dose 20vPnC
Reporting group description:	
Toddlers ≥ 12 to < 24 months of age were randomised to receive 2 doses of 0.5 milliliter (mL) 20vPnC intramuscularly. Dose 1 was administered at Day 1 (Dose 1 Visit) and Dose 2 was administered 56 to 70 days later (Dose 2 Visit).	
Reporting group title	1-Dose 20vPnC
Reporting group description:	
Toddlers ≥ 12 to < 24 months of age were randomised to receive 1 dose of 0.5 mL 20vPnC intramuscularly on Day 1 (Dose 1 Visit).	
Reporting group title	13vPnC Control
Reporting group description:	
Toddlers ≥ 12 to < 24 months of age were randomised to receive 1 dose of 0.5 mL 13vPnC intramuscularly on Day 1 (Dose 1 Visit).	

Reporting group values	2-Dose 20vPnC	1-Dose 20vPnC	13vPnC Control
Number of subjects	121	118	117
Age Categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	121	118	117
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous			
Units: months			
arithmetic mean	12.5	12.6	12.7
standard deviation	± 1.21	± 1.52	± 1.85
Gender Categorical			
Units: Subjects			
Female	60	47	57
Male	61	71	60
Race (NIH/OMB)			
Units: Subjects			
White	120	117	113
Black or African American	1	0	1
Asian	0	1	1
Multiracial	0	0	1
Not reported	0	0	1
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic/Latino	34	36	32
Non-Hispanic/non-Latino	86	82	85

Not reported	1	0	0
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Reporting group values	Total		
Number of subjects	356		
Age Categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	356		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Age Continuous Units: months arithmetic mean standard deviation	-		
Gender Categorical Units: Subjects			
Female	164		
Male	192		
Race (NIH/OMB) Units: Subjects			
White	350		
Black or African American	2		
Asian	2		
Multiracial	1		
Not reported	1		
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic/Latino	102		
Non-Hispanic/non-Latino	253		
Not reported	1		

End points

End points reporting groups

Reporting group title	2-Dose 20vPnC
Reporting group description: Toddlers ≥ 12 to < 24 months of age were randomised to receive 2 doses of 0.5 milliliter (mL) 20vPnC intramuscularly. Dose 1 was administered at Day 1 (Dose 1 Visit) and Dose 2 was administered 56 to 70 days later (Dose 2 Visit).	
Reporting group title	1-Dose 20vPnC
Reporting group description: Toddlers ≥ 12 to < 24 months of age were randomised to receive 1 dose of 0.5 mL 20vPnC intramuscularly on Day 1 (Dose 1 Visit).	
Reporting group title	13vPnC Control
Reporting group description: Toddlers ≥ 12 to < 24 months of age were randomised to receive 1 dose of 0.5 mL 13vPnC intramuscularly on Day 1 (Dose 1 Visit).	

Primary: Percentage of Subjects With Local Reactions Within 7 Days After Last Vaccination

End point title	Percentage of Subjects With Local Reactions Within 7 Days After Last Vaccination ^[1]
End point description: Local reactions included redness, swelling, and pain at the injection site, recorded by parents/legal guardians of subjects in an electronic diary (e-diary). Redness and swelling were measured and recorded in measuring device (caliper) units. 1 measuring device unit = 0.5 centimeter (cm). Redness and swelling were graded as mild (greater than $>$ 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 example, whimpered, winced, protested, or withdrew), moderate (hurt if gently touched, with crying), and severe (caused limitation of limb movement). 95 percent (%) confidence interval (CI) was based on Clopper and Pearson method. Safety analysis set included all subjects who received at least 1 dose of 20vPnC or 13vPnC and had safety data reported after any dose. Here, "Number of subjects Analyzed" signifies the number of subjects with any e-diary data reported after the last vaccination.	
End point type	Primary
End point timeframe: Within 7 days after last vaccination (for reporting arm 2-Dose 20vPnC last vaccination was Dose 2 and for 1-dose 20vPnC and 13vPnC Control it was 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 analysis was planned for this endpoint.	

End point values	2-Dose 20vPnC	1-Dose 20vPnC	13vPnC Control	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	114	118	117	
Units: Percentage of subjects				
number (confidence interval 95%)				
Redness: Any	26.3 (18.5 to 35.4)	29.7 (21.6 to 38.8)	32.5 (24.1 to 41.8)	
Redness: Mild	13.2 (7.6 to 20.8)	18.6 (12.1 to 26.9)	17.9 (11.5 to 26.1)	
Redness: Moderate	12.3 (6.9 to 19.7)	11.0 (6.0 to 18.1)	14.5 (8.7 to 22.2)	
Redness: Severe	0.9 (0.0 to 4.8)	0 (0.0 to 3.1)	0 (0.0 to 3.1)	

Swelling: Any	23.7 (16.2 to 32.6)	21.2 (14.2 to 29.7)	25.6 (18.0 to 34.5)	
Swelling: Mild	14.0 (8.2 to 21.8)	12.7 (7.3 to 20.1)	16.2 (10.1 to 24.2)	
Swelling: Moderate	8.8 (4.3 to 15.5)	8.5 (4.1 to 15.0)	9.4 (4.8 to 16.2)	
Swelling: Severe	0.9 (0.0 to 4.8)	0 (0.0 to 3.1)	0 (0.0 to 3.1)	
Pain at Injection Site: Any	29.8 (21.6 to 39.1)	28.8 (20.8 to 37.9)	31.6 (23.3 to 40.9)	
Pain at Injection Site: Mild	17.5 (11.1 to 25.8)	17.8 (11.4 to 25.9)	26.5 (18.8 to 35.5)	
Pain at Injection Site: Moderate	12.3 (6.9 to 19.7)	11.0 (6.0 to 18.1)	5.1 (1.9 to 10.8)	
Pain at Injection Site: Severe	0 (0.0 to 3.2)	0 (0.0 to 3.1)	0 (0.0 to 3.1)	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Systemic Events Within 7 Days After Last Vaccination

End point title	Percentage of Subjects With Systemic Events Within 7 Days After Last Vaccination ^[2]
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End point description:

Systemic events included fever, decreased appetite, drowsiness/increased sleep & irritability, recorded by parents/legal guardians of subjects using an e-diary. Fever: temperature ≥ 38.0 degree Celsius (C) & categorized 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/prolonged sleeping bouts), moderate (slightly subdued, interfered with daily activity) and severe (disabling, not interested in usual daily activity). Irritability was graded as mild (easily consolable), moderate (required increased attention) and severe (inconsolable, crying could not be comforted). 95% confidence interval (CI) was based on Clopper & Pearson method. Safety analysis set was analyzed. "Number of subjects Analyzed"=number of subjects with any e-diary data reported after the last vaccination.

End point type	Primary
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End point timeframe:

Within 7 days after last vaccination (for reporting arm 2-Dose 20vPnC last vaccination was Dose 2 and for 1-dose 20vPnC and 13vPnC Control it was Dose 1)

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 analysis was planned for this endpoint.

End point values	2-Dose 20vPnC	1-Dose 20vPnC	13vPnC Control	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	114	118	117	
Units: Percentage of subjects				
number (confidence interval 95%)				
Fever: ≥ 38.0 degrees C	9.6 (4.9 to 16.6)	15.3 (9.3 to 23.0)	15.4 (9.4 to 23.2)	
Fever: >38.0 degrees C to 38.4 degrees C	3.5 (1.0 to 8.7)	6.8 (3.0 to 12.9)	10.3 (5.4 to 17.2)	
Fever: >38.4 degrees C to 38.9 degrees C	4.4 (1.4 to 9.9)	3.4 (0.9 to 8.5)	2.6 (0.5 to 7.3)	
Fever: >38.9 degrees C to 40.0 degrees C	1.8 (0.2 to 6.2)	5.1 (1.9 to 10.7)	2.6 (0.5 to 7.3)	

Fever: >40.0 degrees C	0 (0.0 to 3.2)	0 (0.0 to 3.1)	0 (0.0 to 3.1)	
Decreased appetite: Any	25.4 (17.7 to 34.4)	33.1 (24.7 to 42.3)	26.5 (18.8 to 35.5)	
Decreased appetite: Mild	14.9 (8.9 to 22.8)	15.3 (9.3 to 23.0)	12.0 (6.7 to 19.3)	
Decreased appetite: Moderate	10.5 (5.6 to 17.7)	14.4 (8.6 to 22.1)	13.7 (8.0 to 21.3)	
Decreased appetite: Severe	0 (0.0 to 3.2)	3.4 (0.9 to 8.5)	0.9 (0.0 to 4.7)	
Drowsiness/increased sleep: Any	23.7 (16.2 to 32.6)	32.2 (23.9 to 41.4)	31.6 (23.3 to 40.9)	
Drowsiness/increased sleep: Mild	18.4 (11.8 to 26.8)	25.4 (17.9 to 34.3)	21.4 (14.3 to 29.9)	
Drowsiness/increased sleep: Moderate	5.3 (2.0 to 11.1)	5.9 (2.4 to 11.8)	10.3 (5.4 to 17.2)	
Drowsiness/increased sleep: Severe	0 (0.0 to 3.2)	0.8 (0.0 to 4.6)	0 (0.0 to 3.1)	
Irritability: Any	55.3 (45.7 to 64.6)	50.8 (41.5 to 60.2)	46.2 (36.9 to 55.6)	
Irritability: Mild	24.6 (17.0 to 33.5)	15.3 (9.3 to 23.0)	16.2 (10.1 to 24.2)	
Irritability: Moderate	29.8 (21.6 to 39.1)	32.2 (23.9 to 41.4)	29.9 (21.8 to 39.1)	
Irritability: Severe	0.9 (0.0 to 4.8)	3.4 (0.9 to 8.5)	0 (0.0 to 3.1)	

Statistical analyses

No statistical analyses for this end point

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

End point title	Percentage of Subjects With Adverse Events (AEs) From Last Vaccination to 1 Month After Last Vaccination ^[3]
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End point description:

An AE was any untoward medical occurrence in a subject, temporally associated with the use of study intervention, whether or not considered related to the study intervention. 95% CI was based on the Clopper and Pearson method. AEs reported in this endpoint excluded local reactions and systemic events collected from an e-diary. Safety analysis set included all subjects who received at least 1 dose of 20vPnC or 13vPnC and had safety data assessed after any dose. Here, "Number of subjects Analysed" signifies the number of subjects in the specified group that received the last vaccination.

End point type	Primary
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End point timeframe:

From last vaccination to 1 Month after last vaccination (for reporting arm 2-Dose 20vPnC last vaccination was Dose 2 and for 1-dose 20vPnC and 13vPnC Control it was Dose 1)

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 analysis was planned for this endpoint.

End point values	2-Dose 20vPnC	1-Dose 20vPnC	13vPnC Control	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	116	118	117	
Units: Percentage of subjects				
number (confidence interval 95%)	22.4 (15.2 to 31.1)	24.6 (17.1 to 33.4)	25.6 (18.0 to 34.5)	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Serious Adverse Events (SAEs) From Last Vaccination to 1 Month After Last Vaccination

End point title	Percentage of Subjects With Serious Adverse Events (SAEs) From Last Vaccination to 1 Month After Last Vaccination ^[4]
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End point description:

A SAE was any untoward medical occurrence that: resulted in death; required inpatient hospitalization or prolongation of existing hospitalization; resulted in persistent or significant disability/ incapacity; was a congenital anomaly/birth defect; was a suspected transmission via a Pfizer product of an infectious agent, pathogenic or non-pathogenic, was considered serious and other important medical events. 95% CI was based on the Clopper and Pearson method. Safety analysis set included all subjects who received at least 1 dose of 20vPnC or 13vPnC and had safety data assessed after any dose. Here, "Number of subjects Analysed" signifies the number of subjects in the specified group that received the last vaccination.

End point type	Primary
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End point timeframe:

1 Month after last vaccination (for reporting arm 2-Dose 20vPnC last vaccination was Dose 2 and for 1-dose 20vPnC and 13vPnC Control it was Dose 1)

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 analysis was planned for this endpoint.

End point values	2-Dose 20vPnC	1-Dose 20vPnC	13vPnC Control	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	116	118	117	
Units: Percentage of subjects				
number (confidence interval 95%)	0.9 (0.0 to 4.7)	0.8 (0.0 to 4.6)	0.9 (0.0 to 4.7)	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Predefined Serotype-Specific Immunoglobulin G (IgG) Concentrations for the 7 Additional Serotypes 1 Month After Last Vaccination

End point title	Percentage of Subjects With Predefined Serotype-Specific Immunoglobulin G (IgG) Concentrations for the 7 Additional Serotypes 1 Month After Last Vaccination ^[5]
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End point description:

Pneumococcal serotype-specific IgG concentrations were measured for serum samples for 7 additional serotypes: 8, 10A, 11A, 12F, 15B, 22F, 33F. The predefined level was 0.35 microgram per milliliter (mcg/mL) for all 7 additional serotypes. 95% CI was based on the Clopper and Pearson method. Evaluable immunogenicity population included all subjects who were eligible, received vaccinations to

which they were randomized, had at least 1 valid immunogenicity result from 1 month after the last assigned vaccination collected within 27 to 56 days after the dose, had no other major protocol deviations as determined by clinician. "Number of subjects analysed"= subjects in evaluable immunogenicity population. "n"= subjects with valid IgG results for specified serotype.

End point type	Primary
End point timeframe:	
1 Month after last vaccination (for reporting arm 2-Dose 20vPnC last vaccination was Dose 2 and for 1-dose 20vPnC and 13vPnC Control it was 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 analysis was planned for this endpoint.

End point values	2-Dose 20vPnC	1-Dose 20vPnC	13vPnC Control	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	102	108	108	
Units: Percentage of subjects				
number (confidence interval 95%)				
Serotype 8, n=102, 108, 107	100.0 (96.4 to 100.0)	98.1 (93.5 to 99.8)	8.4 (3.9 to 15.4)	
Serotype 10A, n=102, 108, 108	99.0 (94.7 to 100.0)	87.0 (79.2 to 92.7)	1.9 (0.2 to 6.5)	
Serotype 11A, n=102, 108, 108	99.0 (94.7 to 100.0)	96.3 (90.8 to 99.0)	13.0 (7.3 to 20.8)	
Serotype 12F, n=102, 108, 108	91.2 (83.9 to 95.9)	54.6 (44.8 to 64.2)	0.0 (0.0 to 3.4)	
Serotype 15B, n=102, 108, 108	100.0 (96.4 to 100.0)	75.9 (66.7 to 83.6)	6.5 (2.6 to 12.9)	
Serotype 22F, n=102, 108, 108	100.0 (96.4 to 100.0)	94.4 (88.3 to 97.9)	2.8 (0.6 to 7.9)	
Serotype 33F, n=102, 108, 108	99.0 (94.7 to 100.0)	83.3 (74.9 to 89.8)	3.7 (1.0 to 9.2)	

Statistical analyses

No statistical analyses for this end point

Secondary: Serotype-specific IgG Geometric Mean Concentrations (GMC) 1 Month After Last Vaccination

End point title	Serotype-specific IgG Geometric Mean Concentrations (GMC) 1 Month After Last Vaccination
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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 serotypes: 8, 10A, 11A, 12F, 15B, 22F, 33F. Assay results below the LLOQ were set to 0.5*LLOQ. GMC & corresponding 2-sided 95% CIs were calculated by exponentiating mean logarithm of concentration, corresponding 2-sided 95% CIs (based on Student's t distribution). Evaluable immunogenicity population included all subjects who were eligible, received vaccinations to which they were randomized, had at least 1 valid immunogenicity result from 1 month after the last assigned vaccination collected within 27 to 56 days after the dose, had no other major protocol deviations as determined by clinician. Number of Subjects Analysed= subjects in evaluable immunogenicity population. "n"= subjects with valid IgG assay results for specified serotype.

End point type	Secondary
End point timeframe:	
1 Month after last vaccination (for reporting arm 2-Dose 20vPnC last vaccination was Dose 2 and for 1-dose 20vPnC and 13vPnC Control it was Dose 1)	

End point values	2-Dose 20vPnC	1-Dose 20vPnC	13vPnC Control	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	102	108	108	
Units: mcg/mL				
geometric mean (confidence interval 95%)				
Serotype 1, n=102, 108, 108	1.66 (1.39 to 2.00)	2.40 (1.95 to 2.96)	3.38 (2.82 to 4.05)	
Serotype 3, n=102, 108, 108	0.78 (0.65 to 0.93)	0.95 (0.80 to 1.14)	1.24 (1.06 to 1.45)	
Serotype 4, n=102, 108, 108	3.09 (2.63 to 3.63)	4.54 (3.63 to 5.67)	5.67 (4.81 to 6.70)	
Serotype 5, n=102, 108, 108	1.61 (1.36 to 1.92)	2.03 (1.64 to 2.51)	2.46 (2.04 to 2.95)	
Serotype 6A, n=102, 108, 108	8.55 (7.25 to 10.07)	12.45 (10.16 to 15.27)	16.28 (13.48 to 19.66)	
Serotype 6B, n=102, 108, 107	5.17 (4.25 to 6.29)	4.87 (3.60 to 6.60)	6.64 (5.19 to 8.52)	
Serotype 7F, n=102, 108, 108	4.78 (4.15 to 5.49)	4.41 (3.81 to 5.10)	6.32 (5.49 to 7.28)	
Serotype 9V, n=102, 108, 108	3.44 (2.96 to 3.99)	3.94 (3.29 to 4.71)	5.36 (4.55 to 6.31)	
Serotype 14, n=102, 108, 108	5.58 (4.66 to 6.68)	7.37 (5.85 to 9.29)	8.64 (7.01 to 10.64)	
Serotype 18C, n=102, 108, 108	2.84 (2.39 to 3.39)	3.13 (2.62 to 3.74)	3.78 (3.14 to 4.54)	
Serotype 19A, n=102, 108, 108	3.31 (2.80 to 3.90)	6.36 (5.22 to 7.74)	6.89 (5.76 to 8.23)	
Serotype 19F, n=102, 107, 108	5.25 (4.38 to 6.28)	8.78 (7.04 to 10.94)	10.09 (8.33 to 12.22)	
Serotype 23F, n=102, 108, 108	5.06 (4.23 to 6.05)	4.45 (3.58 to 5.53)	6.32 (5.07 to 7.89)	
Serotype 8, n=102, 108, 107	10.16 (8.75 to 11.79)	7.56 (6.22 to 9.19)	0.05 (0.04 to 0.07)	
Serotype 10A, n=102, 108, 108	6.54 (5.17 to 8.28)	1.32 (0.98 to 1.76)	0.01 (0.01 to 0.02)	
Serotype 11A, n=102, 108, 108	4.83 (4.11 to 5.68)	2.72 (2.17 to 3.41)	0.03 (0.02 to 0.04)	
Serotype 12F, n=102, 108, 108	1.72 (1.40 to 2.12)	0.33 (0.25 to 0.45)	0.01 (0.01 to 0.01)	
Serotype 15B, n=102, 108, 108	11.21 (9.39 to 13.38)	0.95 (0.74 to 1.21)	0.03 (0.02 to 0.04)	
Serotype 22F, n=102, 108, 108	15.45 (13.24 to 18.03)	8.66 (6.27 to 11.98)	0.01 (0.00 to 0.01)	
Serotype 33F, n=102, 108, 108	4.94 (4.04 to 6.03)	1.68 (1.21 to 2.34)	0.02 (0.01 to 0.02)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Predefined IgG Concentrations for the 13

Matched Serotypes 1 Month After Last Vaccination

End point title	Percentage of Subjects with Predefined IgG Concentrations for the 13 Matched Serotypes 1 Month After Last Vaccination
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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, 23F. Predefined level was 0.35 mcg/mL for all 13vPnC serotypes except serotypes 5, 6B, and 19A, which had predefined levels of 0.23, 0.10, and 0.12 mcg/mL, respectively. 95% CI was based on the Clopper and Pearson method. Evaluable immunogenicity population included all subjects who were eligible, received vaccinations to which they were randomized, had at least 1 valid immunogenicity result from 1 month after last assigned vaccination collected within 27 to 56 days after dose, had no other major protocol deviations. Number of Subjects Analysed= subjects in evaluable immunogenicity population. "n"=subjects with valid IgG results for specified serotype.

End point type	Secondary
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End point timeframe:

1 Month after last vaccination (for reporting arm 2-Dose 20vPnC last vaccination was Dose 2 and for 1-dose 20vPnC and 13vPnC Control it was Dose 1)

End point values	2-Dose 20vPnC	1-Dose 20vPnC	13vPnC Control	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	102	108	108	
Units: Percentage of subjects				
number (confidence interval 95%)				
Serotype 1, n=102, 108, 108	94.1 (87.6 to 97.8)	94.4 (88.3 to 97.9)	98.1 (93.5 to 99.8)	
Serotype 3, n=102, 108, 108	88.2 (80.4 to 93.8)	87.0 (79.2 to 92.7)	93.5 (87.1 to 97.4)	
Serotype 4, n=102, 108, 108	98.0 (93.1 to 99.8)	99.1 (94.9 to 100.0)	100.0 (96.6 to 100.0)	
Serotype 5, n=102, 108, 108	97.1 (91.6 to 99.4)	96.3 (90.8 to 99.0)	100.0 (96.6 to 100.0)	
Serotype 6A, n=102, 108, 108	100.0 (96.4 to 100.0)	99.1 (94.9 to 100.0)	99.1 (94.9 to 100.0)	
Serotype 6B, n=102, 108, 107	100.0 (96.4 to 100.0)	98.1 (93.5 to 99.8)	100.0 (96.6 to 100.0)	
Serotype 7F, n=102, 108, 108	100.0 (96.4 to 100.0)	100.0 (96.6 to 100.0)	100.0 (96.6 to 100.0)	
Serotype 9V, n=102, 108, 108	100.0 (96.4 to 100.0)	99.1 (94.9 to 100.0)	100.0 (96.6 to 100.0)	
Serotype 14, n=102, 108, 108	100.0 (96.4 to 100.0)	99.1 (94.9 to 100.0)	99.1 (94.9 to 100.0)	
Serotype 18C, n=102, 108, 108	100.0 (96.4 to 100.0)	98.1 (93.5 to 99.8)	99.1 (94.9 to 100.0)	
Serotype 19A, n=102, 108, 108	100.0 (96.4 to 100.0)	100.0 (96.6 to 100.0)	100.0 (96.6 to 100.0)	
Serotype 19F, n=102, 107, 108	100.0 (96.4 to 100.0)	99.1 (94.9 to 100.0)	100.0 (96.6 to 100.0)	
Serotype 23F, n=102, 108, 108	99.0 (94.7 to 100.0)	99.1 (94.9 to 100.0)	97.2 (92.1 to 99.4)	

Statistical analyses

Secondary: Serotype-specific opsonophagocytic activity (OPA) Geometric Mean Titers (GMTs) 1 Month After Last Vaccination

End point title	Serotype-specific opsonophagocytic activity (OPA) Geometric Mean Titers (GMTs) 1 Month After Last Vaccination
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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 randomly selected subsets of subjects at 1 month after Dose 2. Results were expressed as OPA titers. GMTs and 2-sided CIs were calculated by exponentiating the mean logarithm of the titers and the corresponding CIs based on the Student's t distribution. Evaluable immunogenicity population included all subjects who were eligible, received vaccinations to which they were randomized, had at least 1 valid immunogenicity result from 1 month after the last assigned vaccination collected within 27 to 56 days after the dose, had no other major protocol deviations as determined by clinician. "Number of Subjects Analysed"= subjects in evaluable immunogenicity population with any valid OPA titers for the specified group, "n"= subjects with valid OPA assay results for specified serotype.

End point type	Secondary
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End point timeframe:

1 Month after last vaccination (for reporting arm 2-Dose 20vPnC last vaccination was Dose 2 and for 1-dose 20vPnC and 13vPnC Control it was Dose 1)

End point values	2-Dose 20vPnC	1-Dose 20vPnC	13vPnC Control	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	36	33	34	
Units: Titers				
geometric mean (confidence interval 95%)				
Serotype 1, n=25, 32, 34	46 (26 to 82)	79 (47 to 133)	105 (68 to 162)	
Serotype 3, n=25, 33, 32	131 (106 to 163)	101 (72 to 142)	128 (93 to 176)	
Serotype 4, n=30, 31, 32	348 (178 to 681)	425 (213 to 845)	541 (298 to 984)	
Serotype 5, n=26, 33, 34	46 (30 to 69)	77 (52 to 114)	73 (52 to 104)	
Serotype 6A, n=25, 33, 34	1470 (1030 to 2096)	1156 (768 to 1739)	1796 (1286 to 2508)	
Serotype 6B, n=26, 32, 33	698 (437 to 1114)	452 (275 to 743)	790 (459 to 1357)	
Serotype 7F, n=26, 30, 29	1415 (844 to 2371)	1212 (755 to 1945)	1367 (790 to 2365)	
Serotype 9V, n=28, 30, 31	1719 (928 to 3185)	1792 (1015 to 3166)	1930 (1048 to 3556)	
Serotype 14, n=23, 30, 32	844 (474 to 1501)	1245 (837 to 1852)	558 (308 to 1011)	
Serotype 18C, n=29, 31, 31	1861 (1115 to 3106)	1047 (583 to 1882)	1149 (684 to 1930)	
Serotype 19A, n=26, 30, 31	512 (283 to 925)	731 (401 to 1332)	973 (560 to 1688)	
Serotype 19F, n=25, 32, 34	473 (257 to 873)	470 (285 to 775)	595 (363 to 975)	
Serotype 23F, n=28, 30, 32	727 (382 to 1382)	472 (255 to 876)	721 (439 to 1186)	
Serotype 8, n=33, 32, 33	3446 (2282 to 5203)	1609 (989 to 2617)	76 (42 to 137)	

Serotype 10A, n=36, 33, 32	6783 (4555 to 10100)	2506 (1425 to 4407)	64 (40 to 104)	
Serotype 11A, n=36, 30, 30	3827 (1975 to 7414)	3416 (1523 to 7665)	235 (99 to 562)	
Serotype 12F, n=32, 31, 32	17398 (11121 to 27218)	7346 (3895 to 13855)	64 (34 to 122)	
Serotype 15B, n=35, 29, 34	10024 (6200 to 16206)	3898 (1867 to 8136)	58 (24 to 143)	
Serotype 22F, n=35, 31, 33	11820 (7993 to 17480)	6117 (3289 to 11376)	28 (13 to 61)	
Serotype 33F, n=33, 32, 32	43671 (28126 to 67809)	15355 (9431 to 24998)	694 (432 to 1115)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Local reactions & Systemic events: Within 7 days after each vaccination; SAEs & non-SAEs: from study dose to 1 month (M) after last dose. Results are summarized by: 2-Dose 20vPnC Dose(D) 1 to D2, 2-Dose 20vPnC (D2 to 1M after), 1-Dose 20vPnC, 13vPnC Control

Adverse event reporting additional description:

Same event may appear as both SAE & non-SAE. But what is presented are distinct events. Event may be classified as serious in 1 subject & non-serious in another, or 1 subject may have experienced both during study. Local reactions/systemic events collected by systematic assessment (SA); SAE/non-SAEs collected by non-SA. Safety analysis set analysed.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups

Reporting group title	2-Dose 20vPnC Dose 1 to Dose 2
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Reporting group description:

Toddlers ≥ 12 to < 24 months of age were randomized to receive 2 doses of 0.5 mL 20vPnC intramuscularly. Dose 1 was administered at Day 1 (Dose 1 Visit) and Dose 2 was administered 56 to 70 days later (Dose 2 Visit).

Reporting group title	2-Dose 20vPnC
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Reporting group description:

Toddlers ≥ 12 to < 24 months of age were randomized to receive 2 doses of 0.5 mL 20vPnC intramuscularly. Dose 1 was administered at Day 1 (Dose 1 Visit) and Dose 2 was administered 56 to 70 days later (Dose 2 Visit).

Reporting group title	1-Dose 20vPnC
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Reporting group description:

Toddlers ≥ 12 to < 24 months of age were randomized to receive 1 dose of 0.5 mL 20vPnC intramuscularly on Day 1 (Dose 1 Visit).

Reporting group title	13vPnC Control
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Reporting group description:

Toddlers ≥ 12 to < 24 months of age were randomized to receive 1 dose of 0.5 mL 20vPnC intramuscularly on Day 1 (Dose 1 Visit).

Serious adverse events	2-Dose 20vPnC Dose 1 to Dose 2	2-Dose 20vPnC	1-Dose 20vPnC
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 121 (3.31%)	1 / 116 (0.86%)	1 / 118 (0.85%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Thermal burn			
subjects affected / exposed	0 / 121 (0.00%)	0 / 116 (0.00%)	1 / 118 (0.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Nervous system disorders			
Febrile convulsion			
subjects affected / exposed	1 / 121 (0.83%)	0 / 116 (0.00%)	0 / 118 (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
Respiratory, thoracic and mediastinal disorders			
Wheezing			
subjects affected / exposed	0 / 121 (0.00%)	0 / 116 (0.00%)	0 / 118 (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
Bronchospasm			
subjects affected / exposed	1 / 121 (0.83%)	0 / 116 (0.00%)	0 / 118 (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
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 121 (0.00%)	1 / 116 (0.86%)	0 / 118 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Lower respiratory tract infection			
subjects affected / exposed	1 / 121 (0.83%)	1 / 116 (0.86%)	0 / 118 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	1 / 121 (0.83%)	0 / 116 (0.00%)	0 / 118 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	1 / 121 (0.83%)	0 / 116 (0.00%)	0 / 118 (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

Serious adverse events	13vPnC Control		
Total subjects affected by serious adverse events			

subjects affected / exposed	1 / 117 (0.85%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Thermal burn			
subjects affected / exposed	0 / 117 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Febrile convulsion			
subjects affected / exposed	0 / 117 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Wheezing			
subjects affected / exposed	1 / 117 (0.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bronchospasm			
subjects affected / exposed	0 / 117 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 117 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Lower respiratory tract infection			
subjects affected / exposed	0 / 117 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			

subjects affected / exposed	0 / 117 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bronchitis			
subjects affected / exposed	0 / 117 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	2-Dose 20vPnC Dose 1 to Dose 2	2-Dose 20vPnC	1-Dose 20vPnC
Total subjects affected by non-serious adverse events			
subjects affected / exposed	93 / 121 (76.86%)	91 / 116 (78.45%)	90 / 118 (76.27%)
Nervous system disorders			
Hypersomnia (INCREASED SLEEP)			
alternative assessment type: Systematic			
subjects affected / exposed	39 / 121 (32.23%)	27 / 116 (23.28%)	38 / 118 (32.20%)
occurrences (all)	39	27	38
General disorders and administration site conditions			
Injection site erythema (REDNESS)			
alternative assessment type: Systematic			
subjects affected / exposed	40 / 121 (33.06%)	30 / 116 (25.86%)	35 / 118 (29.66%)
occurrences (all)	40	30	35
Injection site swelling (SWELLING)			
alternative assessment type: Systematic			
subjects affected / exposed	27 / 121 (22.31%)	27 / 116 (23.28%)	25 / 118 (21.19%)
occurrences (all)	27	27	25
Pyrexia (FEVER)			
alternative assessment type: Systematic			
subjects affected / exposed	20 / 121 (16.53%)	11 / 116 (9.48%)	18 / 118 (15.25%)
occurrences (all)	20	11	18
Injection site pain (PAIN)			
alternative assessment type: Systematic			

subjects affected / exposed occurrences (all)	33 / 121 (27.27%) 33	34 / 116 (29.31%) 34	34 / 118 (28.81%) 34
Psychiatric disorders Irritability alternative assessment type: Systematic subjects affected / exposed occurrences (all)	70 / 121 (57.85%) 70	63 / 116 (54.31%) 63	60 / 118 (50.85%) 60
Infections and infestations Upper respiratory tract infection subjects affected / exposed occurrences (all)	18 / 121 (14.88%) 22	9 / 116 (7.76%) 10	13 / 118 (11.02%) 13
Metabolism and nutrition disorders Decreased appetite (DECREASED APPETITE) alternative assessment type: Systematic subjects affected / exposed occurrences (all)	37 / 121 (30.58%) 37	29 / 116 (25.00%) 29	39 / 118 (33.05%) 39

Non-serious adverse events	13vPnC Control		
Total subjects affected by non-serious adverse events subjects affected / exposed	98 / 117 (83.76%)		
Nervous system disorders Hypersomnia (INCREASED SLEEP) alternative assessment type: Systematic subjects affected / exposed occurrences (all)	37 / 117 (31.62%) 37		
General disorders and administration site conditions Injection site erythema (REDNESS) alternative assessment type: Systematic subjects affected / exposed occurrences (all) Injection site swelling (SWELLING) alternative assessment type: Systematic subjects affected / exposed occurrences (all) Pyrexia (FEVER) alternative assessment type: Systematic	38 / 117 (32.48%) 38 30 / 117 (25.64%) 30 		

subjects affected / exposed occurrences (all) Injection site pain (PAIN) alternative assessment type: Systematic subjects affected / exposed occurrences (all)	18 / 117 (15.38%) 18 37 / 117 (31.62%) 37		
Psychiatric disorders Irritability alternative assessment type: Systematic subjects affected / exposed occurrences (all)	54 / 117 (46.15%) 54		
Infections and infestations Upper respiratory tract infection subjects affected / exposed occurrences (all)	9 / 117 (7.69%) 10		
Metabolism and nutrition disorders Decreased appetite (DECREASED APPETITE) alternative assessment type: Systematic subjects affected / exposed occurrences (all)	31 / 117 (26.50%) 31		

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