Clinical trial results:
A Phase 3, Multicenter, Single-arm, Open- Label Study to Assess the Safety, Tolerability, and Immunogenicity of a Single Dose of 13-Valent Pneumococcal Conjugate Vaccine in Japanese Subjects Aged 6 to 64 Years Who are Considered to be at Increased Risk of Pneumococcal Disease and Who are Naive to Pneumococcal Vaccines

Summary

EudraCT number	2018-003054-24
Trial protocol	Outside EU/EEA
Global end of trial date	16 November 2018

Results information

Result version number	v1
This version publication date	30 May 2019
First version publication date	30 May 2019

Trial information

Trial identification

Sponsor protocol code	B1851172

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03571607
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer, Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, 10017
Public contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., +1 18007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., +1 18007181021, ClinicalTrials.gov_Inquiries@pfizer.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	16 November 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	16 November 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the safety and tolerability of a single dose of 13-valent pneumococcal conjugate vaccine (13vPnC) as measured by the incidence of local reactions, systemic events, adverse events (AEs), and serious adverse events (SAEs).

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	12 July 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Japan: 206
Worldwide total number of subjects	206
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)	0
Children (2-11 years)	18
Adolescents (12-17 years)	35
Adults (18-64 years)	153
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The study was conducted in Japan for a total of 206 subjects between 12 July 2018 and 16 November 2018.

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	13vPnC: 6 to <18 Years

Arm description:

Subjects aged between 6 to less than (<) 18 years received a single 0.5 milliliter (mL) dose of 13vPnC intramuscularly on Day 1.

Arm type	Experimental
Investigational medicinal product name	13vPnC
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 0.5 mL 13vPnC conjugate vaccine intramuscularly on Day 1.

Arm title	13vPnC: 18 to <65 Years

Arm description:

Subjects aged between 18 to <65 years received a single 0.5 mL dose of 13vPnC intramuscularly on Day 1.

Arm type	Experimental
Investigational medicinal product name	13vPnC
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 0.5 mL 13vPnC conjugate vaccine intramuscularly on Day 1.

Number of subjects in period 1	13vPnC: 6 to <18 Years	13vPnC: 18 to <65 Years
Started	53	153
Vaccinated	53	153
Completed	53	153

Baseline characteristics

Reporting groups	
Reporting group title	13vPnC: 6 to <18 Years
Reporting group description:	
Subjects aged between 6 to less than (<) 18 years received a single 0.5 milliliter (mL) dose of 13vPnC intramuscularly on Day 1.	
Reporting group title	13vPnC: 18 to <65 Years
Reporting group description:	
Subjects aged between 18 to <65 years received a single 0.5 mL dose of 13vPnC intramuscularly on Day 1.	

Reporting group values	13vPnC: 6 to <18 Years	13vPnC: 18 to <65 Years	Total
Number of subjects	53	153	206
Age categorical Units: Subjects			
6 to <18 years	53	0	53
18 to <65 years	0	153	153
Age Continuous Units: years			
arithmetic mean	12.7	49.0	
standard deviation	± 2.66	± 10.12	-
Sex: Female, Male Units: Subjects			
Female	22	77	99
Male	31	76	107
Ethnicity, Customized Units: Subjects			
Non-Hispanic/non-Latino/not of Spanish origin|	53	153	206
Race, Customized Units: Subjects			
Asian	53	153	206

Subject analysis sets	
Subject analysis set title	13vPnC: All Subjects
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
All subjects aged between 6 to <65 years received a single 0.5 mL dose of 13vPnC intramuscularly on Day 1.	

Reporting group values	13vPnC: All Subjects		
Number of subjects	206		
Age categorical Units: Subjects			
6 to <18 years			
18 to <65 years			

Age Continuous Units: years arithmetic mean standard deviation	 39.6 ± 18.18		
Sex: Female, Male Units: Subjects			
Female Male	99 107		
Ethnicity, Customized Units: Subjects			
Non-Hispanic/non-Latino/not of Spanish origin|	206		
Race, Customized Units: Subjects			
Asian	206		

End points

End points reporting groups

Reporting group title	13vPnC: 6 to <18 Years
Reporting group description:	
Subjects aged between 6 to less than (<) 18 years received a single 0.5 milliliter (mL) dose of 13vPnC intramuscularly on Day 1.	
Reporting group title	13vPnC: 18 to <65 Years
Reporting group description:	
Subjects aged between 18 to <65 years received a single 0.5 mL dose of 13vPnC intramuscularly on Day 1.	
Subject analysis set title	13vPnC: All Subjects
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
All subjects aged between 6 to <65 years received a single 0.5 mL dose of 13vPnC intramuscularly on Day 1.	

Primary: Percentage of Subjects Reporting Pre-Specified Local Reactions Within 7 Days After Vaccination in Subjects Aged Between 6 to <18 Years

End point title	Percentage of Subjects Reporting Pre-Specified Local Reactions Within 7 Days After Vaccination in Subjects Aged Between 6 to <18 Years[1][2]
End point description:	
Local reactions were recorded using an electronic daily diary. Local reactions included redness, swelling and pain at injection site. Redness and swelling were graded as mild (0.5 to 2.0 cm), moderate (greater than [>] 2.0 to 7.0 cm) and severe (>7.0 cm) for subjects aged 6 to <12 years, and as mild (2.5 to 5.0 cm), moderate (>5.0 to 10.0 cm) and, severe (>10.0 cm) for subjects aged 12 to <18 years. Pain at injection site was graded as mild (did not interfere with activity), moderate (interfered with activity), and severe (prevented daily activity). Safety analysis set included all subjects who received 1 dose of study vaccine. Here, "n" signifies subjects evaluable for each specified category.	
End point type	Primary
End point timeframe:	
Day 1 up to Day 7	

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 was planned to be analyzed for this endpoint.

[2] - 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 analyzed only for reporting arm: "13vPnC: 6 to <18 Years".

End point values	13vPnC: 6 to <18 Years			
Subject group type	Reporting group			
Number of subjects analysed	53			
Units: percentage of subjects				
number (confidence interval 95%)				
Redness: Any (n= 47)	21.3 (10.7 to 35.7)			
Redness: Mild (n= 47)	10.6 (3.5 to 23.1)			
Redness: Moderate (n= 47)	10.6 (3.5 to 23.1)			
Redness: Severe (n= 47)	0.0 (0.0 to 7.5)			
Swelling: Any (n= 47)	34.0 (20.9 to 49.3)			

Swelling: Mild (n= 47)	14.9 (6.2 to 28.3)			
Swelling: Moderate (n= 47)	17.0 (7.6 to 30.8)			
Swelling: Severe (n= 47)	2.1 (0.1 to 11.3)			
Pain at the injection site: Any (n= 52)	78.8 (65.3 to 88.9)			
Pain at the injection site: Mild (n= 52)	57.7 (43.2 to 71.3)			
Pain at the injection site: Moderate (n= 52)	21.2 (11.1 to 34.7)			
Pain at the injection site: Severe (n= 52)	0.0 (0.0 to 6.8)			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Reporting Pre-Specified Local Reactions Within 14 Days After Vaccination in Subjects Aged Between 18 to <65 Years

End point title	Percentage of Subjects Reporting Pre-Specified Local Reactions Within 14 Days After Vaccination in Subjects Aged Between 18 to <65 Years[3][4]

End point description:

Local reactions were recorded using an electronic daily diary. Local reactions included redness, swelling and pain at injection site. Redness and swelling were graded as mild (2.5 to 5.0 cm), moderate (>5.0 to 10.0 cm) and, severe (>10.0 cm). Pain at injection site was graded as mild (did not interfere with activity), moderate (interfered with activity), and severe (prevented daily activity). Safety analysis set included all subjects who received 1 dose of study vaccine. Here, "n" signifies subjects evaluable for each specified category.

End point type	Primary

End point timeframe:

Day 1 up to Day 14

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: No statistical analysis was planned to be analyzed for this endpoint.

[4] - 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 analyzed only for reporting arm: "13vPnC: 18 to <65 Years".

End point values	13vPnC: 18 to <65 Years			
Subject group type	Reporting group			
Number of subjects analysed	153			
Units: percentage of subjects				
number (confidence interval 95%)				
Redness: Any (n= 135)	7.4 (3.6 to 13.2)			
Redness: Mild (n= 135)	5.2 (2.1 to 10.4)			
Redness: Moderate (n= 135)	2.2 (0.5 to 6.4)			
Redness: Severe (n= 135)	0.0 (0.0 to 2.7)			

Swelling: Any (n= 136)	12.5 (7.5 to 19.3)			
Swelling: Mild (n= 136)	5.1 (2.1 to 10.3)			
Swelling: Moderate (n= 136)	7.4 (3.6 to 13.1)			
Swelling: Severe (n= 136)	0.0 (0.0 to 2.7)			
Pain at the injection site: Any (n= 145)	66.2 (57.9 to 73.8)			
Pain at the injection site: Mild (n= 145)	53.8 (45.3 to 62.1)			
Pain at the injection site: Moderate (n= 145)	11.0 (6.4 to 17.3)			
Pain at the injection site: Severe (n= 145)	1.4 (0.2 to 4.9)			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Reporting Systemic Events and use of Antipyretic or Pain Medication Within 7 Days After Vaccination in Subjects Aged Between 6 to <18 Years

End point title	Percentage of Subjects Reporting Systemic Events and use of Antipyretic or Pain Medication Within 7 Days After Vaccination in Subjects Aged Between 6 to <18 Years[5][6]

End point description:

Systemic events included fever, vomiting, diarrhea, headache, fatigue, muscle and joint pain, and were recorded by using an e-diary. Use of antipyretic or pain medication was also collected by using an e-diary. Fever was graded as 37.5 to 38.4 degree C, 38.5 to 38.9 degree C, 39.0 to 40.0 degree C and >40.0 degree C. Vomiting was graded as mild (1-2 times in 24 hours), moderate (>2 times in 24 hours) and severe (required intravenous hydration). Diarrhea was graded as mild (2-3 loose stools in 24 hours), moderate (4-5 loose stools in 24 hours) and severe (greater than or equals to [>=] 6 loose stools in 24 hours). Headache, fatigue, muscle pain and joint pain were graded as mild (no interference with activity), moderate (some interference with activity) and severe (significant, prevented daily activity). Safety analysis set included all subjects who received 1 dose of study vaccine. Here, "n" signifies subjects evaluable for each specified category.

End point type	Primary

End point timeframe:

Day 1 up to Day 7

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: No statistical analysis was planned to be analyzed for this endpoint.

[6] - 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 analyzed only for reporting arm: "13vPnC: 6 to <18 Years".

End point values	13vPnC: 6 to <18 Years			
Subject group type	Reporting group			
Number of subjects analysed	53			
Units: percentage of subjects				
number (confidence interval 95%)				
Fever: 37.5 degree C to 38.4 degree C (n= 48)	12.5 (4.7 to 25.2)			

Fever: 38.5 degree C to 38.9 degree C (n= 48)	2.1 (0.1 to 11.1)			
Fever: 39.0 degree C to 40.0 degree C (n= 48)	0.0 (0.0 to 7.4)			
Fever: >40.0 degree C (n= 48)	0.0 (0.0 to 7.4)			
Fatigue: Any (n= 48)	37.5 (24.0 to 52.6)			
Fatigue: Mild (n= 48)	25.0 (13.6 to 39.6)			
Fatigue: Moderate (n= 48)	10.4 (3.5 to 22.7)			
Fatigue: Severe (n= 48)	2.1 (0.1 to 11.1)			
Headache: Any (n= 49)	24.5 (13.3 to 38.9)			
Headache: Mild (n= 49)	16.3 (7.3 to 29.7)			
Headache: Moderate (n= 49)	6.1 (1.3 to 16.9)			
Headache: Severe (n= 49)	2.0 (0.1 to 10.9)			
Vomiting: Any (n= 47)	0.0 (0.0 to 7.5)			
Vomiting: Mild (n= 47)	0.0 (0.0 to 7.5)			
Vomiting: Moderate (n= 47)	0.0 (0.0 to 7.5)			
Vomiting: Severe (n= 47)	0.0 (0.0 to 7.5)			
Diarrhea: Any (n= 48)	8.3 (2.3 to 20.0)			
Diarrhea: Mild (n= 48)	8.3 (2.3 to 20.0)			
Diarrhea: Moderate (n= 48)	0.0 (0.0 to 7.4)			
Diarrhea: Severe (n= 48)	0.0 (0.0 to 7.4)			
Muscle pain: Any (n= 49)	30.6 (18.3 to 45.4)			
Muscle pain: Mild (n= 49)	26.5 (14.9 to 41.1)			
Muscle pain: Moderate (n= 49)	4.1 (0.5 to 14.0)			
Muscle pain: Severe (n= 49)	0.0 (0.0 to 7.3)			
Joint pain: Any (n= 48)	6.3 (1.3 to 17.2)			
Joint pain: Mild (n= 48)	4.2 (0.5 to 14.3)			
Joint pain: Moderate (n= 48)	2.1 (0.1 to 11.1)			
Joint pain: Severe (n= 48)	0.0 (0.0 to 7.4)			
Use of antipyretic or pain medication (n= 47)	6.4 (1.3 to 17.5)			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Reporting Systemic Events and use of Antipyretic or Pain Medication Within 14 Days After Vaccination in Subjects Aged Between 18 to <65 Years

End point title	Percentage of Subjects Reporting Systemic Events and use of

	Antipyretic or Pain Medication Within 14 Days After Vaccination in Subjects Aged Between 18 to <65 Years[7][8]

End point description:

Systemic events included fever, vomiting, diarrhea, headache, fatigue, muscle and joint pain, and were recorded by using an e-diary. Use of antipyretic or pain medication was also collected by using an e-diary. Fever was graded as 37.5 to 38.4 degree C, 38.5 to 38.9 degree C, 39.0 to 40.0 degree C and >40.0 degree C. Vomiting was graded as mild (1-2 times in 24 hours), moderate (>2 times in 24 hours) and severe (required intravenous hydration). Diarrhea was graded as mild (2-3 loose stools in 24 hours), moderate (4-5 loose stools in 24 hours) and severe (>=6 loose stools in 24 hours). Headache, fatigue, muscle pain and joint pain were graded as mild (no interference with activity), moderate (some interference with activity) and severe (significant, prevented daily activity). Safety analysis set included all subjects who received 1 dose of study vaccine. Here, "n" signifies subjects evaluable for each specified category.

End point type	Primary

End point timeframe:

Day 1 up to Day 14

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 was planned to be analyzed for this endpoint.

[8] - 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 analyzed only for reporting arm: "13vPnC: 18 to <65 Years".

End point values	13vPnC: 18 to <65 Years			
Subject group type	Reporting group			
Number of subjects analysed	153			
Units: percentage of subjects				
number (confidence interval 95%)				
Fever: 37.5 degree C to 38.4 degree C (n= 134)	6.0 (2.6 to 11.4)			
Fever: 38.5 degree C to 38.9 degree C (n= 134)	0.0 (0.0 to 2.7)			
Fever: 39.0 degree C to 40.0 degree C (n= 134)	0.0 (0.0 to 2.7)			
Fever: >40.0 degree C (n= 134)	0.0 (0.0 to 2.7)			
Fatigue: Any (n= 142)	33.1 (25.4 to 41.5)			
Fatigue: Mild (n= 142)	25.4 (18.4 to 33.3)			
Fatigue: Moderate (n= 142)	7.7 (3.9 to 13.4)			
Fatigue: Severe (n= 142)	0.0 (0.0 to 2.6)			
Headache: Any (n= 141)	23.4 (16.7 to 31.3)			
Headache: Mild (n= 141)	19.1 (13.0 to 26.6)			
Headache: Moderate (n= 141)	4.3 (1.6 to 9.0)			
Headache: Severe (n= 141)	0.0 (0.0 to 2.6)			
Vomiting: Any (n= 136)	1.5 (0.2 to 5.2)			
Vomiting: Mild (n= 136)	1.5 (0.2 to 5.2)			
Vomiting: Moderate (n= 136)	0.0 (0.0 to 2.7)			
Vomiting: Severe (n= 136)	0.0 (0.0 to 2.7)			
Diarrhea: Any (n= 141)	18.4 (12.4 to 25.8)			
Diarrhea: Mild (n= 141)	15.6 (10.0 to 22.7)			

Diarrhea: Moderate (n= 141)	2.1 (0.4 to 6.1)			
Diarrhea: Severe (n= 141)	0.7 (0.0 to 3.9)			
Muscle pain: Any (n= 139)	27.3 (20.1 to 35.5)			
Muscle pain: Mild (n= 139)	20.9 (14.4 to 28.6)			
Muscle pain: Moderate (n= 139)	5.8 (2.5 to 11.0)			
Muscle pain: Severe (n= 139)	0.7 (0.0 to 3.9)			
Joint pain: Any (n= 138)	13.8 (8.5 to 20.7)			
Joint pain: Mild (n= 138)	9.4 (5.1 to 15.6)			
Joint pain: Moderate (n= 138)	3.6 (1.2 to 8.3)			
Joint pain: Severe (n= 138)	0.7 (0.0 to 4.0)			
Use of antipyretic or pain medication (n= 134)	8.2 (4.2 to 14.2)			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Reporting Adverse Events (AEs) and Serious Adverse Events (SAEs)

End point title	Percentage of Subjects Reporting Adverse Events (AEs) and Serious Adverse Events (SAEs)[9]

End point description:

An AE was any untoward medical occurrence in a subjects who received study vaccine without regard to possibility of causal relationship. An SAE is any untoward medical occurrence at any dose that results in death; is life-threatening (immediate risk of death); requires inpatient hospitalization or prolongation of existing hospitalization; results in persistent or significant disability/incapacity (substantial disruption of the ability to conduct normal life functions); results in congenital anomaly/birth defect. Safety analysis set included all subjects who received 1 dose of study vaccine.

End point type	Primary

End point timeframe:

signing of informed consent form (Day 1) up to Day 43

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: No statistical analysis was planned to be analyzed for this endpoint.

End point values	13vPnC: All Subjects			
Subject group type	Subject analysis set			
Number of subjects analysed	206			
Units: percentage of subjects				
number (not applicable)				
AEs	16			
SAEs	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Serotype-specific Immunoglobulin G (IgG) Geometric Mean Concentrations (GMCs) at Pre-vaccination and 1 Month After Vaccination

End point title	Serotype-specific Immunoglobulin G (IgG) Geometric Mean Concentrations (GMCs) at Pre-vaccination and 1 Month After Vaccination

End point description:

Pneumococcal IgG antibody against each of the 13 pneumococcal serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F) was measured centrally using direct binding Luminex assay. Results were expressed as IgG concentrations. IgG concentrations were logarithmically transformed for analysis; geometric means calculated and expressed as geometric mean concentrations (GMCs). Two (2)-sided 95% CIs were constructed by back transformation of the CI for the mean of the logarithmically transformed assay results computed based on the Student t distribution. Evaluable immunogenicity population: eligible subjects who received the study vaccine and took no prohibited vaccines, had blood drawn within the specified time frame 1 month after vaccination with at least 1 valid and determinate assay result (OPA titer or IgG concentration) for at least 1 serotype 1 month after vaccination and had no major protocol violations.

End point type	Secondary

End point timeframe:

Pre-vaccination and 1 month after vaccination

End point values	13vPnC: All Subjects			
Subject group type	Subject analysis set			
Number of subjects analysed	206			
Units: microgram per milliliter (mcg/mL)				
geometric mean (confidence interval 95%)				
Pre-vaccination; Serotype 1	0.132 (0.109 to 0.161)			
1 month after vaccination; Serotype 1	4.427 (3.423 to 5.726)			
Pre-vaccination; Serotype 3	0.115 (0.094 to 0.141)			
1 month after vaccination; Serotype 3	0.531 (0.437 to 0.646)			
Pre-vaccination; Serotype 4	0.055 (0.045 to 0.068)			
1 month after vaccination; Serotype 4	1.826 (1.387 to 2.404)			
Pre-vaccination; Serotype 5	0.058 (0.046 to 0.075)			
1 month after vaccination; Serotype 5	2.779 (1.972 to 3.915)			
Pre-vaccination; Serotype 6A	0.173 (0.133 to 0.224)			
1 month after vaccination; Serotype 6A	4.070 (2.915 to 5.684)			
Pre-vaccination; Serotype 6B	0.105 (0.080 to 0.138)			
1 month after vaccination; Serotype 6B	2.354 (1.631 to 3.396)			
Pre-vaccination; Serotype 7F	0.117 (0.092 to 0.150)			
1 month after vaccination; Serotype 7F	4.670 (3.629 to 6.010)			

Pre-vaccination; Serotype 9V	0.067 (0.054 to 0.082)			
1 month after vaccination; Serotype 9V	1.483 (1.131 to 1.944)			
Pre-vaccination; Serotype 14	0.335 (0.252 to 0.447)			
1 month after vaccination; Serotype 14	7.769 (5.844 to 10.328)			
Pre-vaccination; Serotype 18C	0.168 (0.131 to 0.216)			
1 month after vaccination; Serotype 18C	5.187 (4.026 to 6.682)			
Pre-vaccination; Serotype 19A	0.496 (0.391 to 0.629)			
1 month after vaccination; Serotype 19A	7.616 (5.786 to 10.026)			
Pre-vaccination; Serotype 19F	0.217 (0.171 to 0.275)			
1 month after vaccination; Serotype 19F	4.315 (3.241 to 5.744)			
Pre-vaccination; Serotype 23F	0.181 (0.143 to 0.228)			
1 month after vaccination; Serotype 23F	6.283 (4.524 to 8.727)			

Statistical analyses

No statistical analyses for this end point

Secondary: GMFRs in Serotype-specific IgG From Before Vaccination to 1 Month After Vaccination

End point title	GMFRs in Serotype-specific IgG From Before Vaccination to 1 Month After Vaccination

End point description:

IgG GMFRs were calculated along with corresponding 2-sided 95% CIs for pneumococcal serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F. GMFRs were computed as the fold rise in concentrations at 1 month after vaccination compared to baseline (pre-vaccination). The CIs for GMFRs were back transformations of a CI based on the Student t distribution for the mean difference of the log-transformed assay results before vaccination and 1 month after vaccination. Evaluable immunogenicity population: eligible subjects who received the study vaccine and took no prohibited vaccines, had blood drawn within the specified time frame 1 month after vaccination with at least 1 valid and determinate assay result (OPA titer or IgG concentration) for at least 1 serotype 1 month after vaccination and had no major protocol violations.

End point type	Secondary

End point timeframe:

Pre-vaccination to 1 month after vaccination

End point values	13vPnC: All Subjects			
Subject group type	Subject analysis set			
Number of subjects analysed	206			
Units: fold rise				
geometric mean (confidence interval 95%)				
Serotype 1	33.445 (26.374 to 42.413)			
Serotype 3	4.605 (3.839 to 5.524)			
Serotype 4	32.960 (25.331 to 42.886)			
Serotype 5	47.565 (36.867 to 61.368)			
Serotype 6A	23.587 (18.010 to 30.890)			
Serotype 6B	22.421 (17.045 to 29.493)			
Serotype 7F	39.843 (31.473 to 50.438)			
Serotype 9V	22.232 (17.426 to 28.362)			
Serotype 14	23.161 (17.179 to 31.227)			
Serotype 18C	30.833 (24.008 to 39.597)			
Serotype 19A	15.354 (12.116 to 19.459)			
Serotype 19F	19.892 (15.552 to 25.443)			
Serotype 23F	34.809 (26.436 to 45.833)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: signing of informed consent form (Day 1) up to Day 43	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	21.1
Reporting groups	
Reporting group title	13vPnC: 6 to <18 Years
Reporting group description: Subjects aged between 6 to <18 years received a single 0.5 mL dose of 13vPnC intramuscularly on Day 1.	
Reporting group title	13vPnC: 18 to <65 Years
Reporting group description: Subjects aged between 18 to <65 years received a single 0.5 mL dose of 13vPnC intramuscularly on Day 1.	
Reporting group title	13vPnC: All Subjects
Reporting group description: All subjects aged between 6 to <65 years received a single 0.5 mL dose of 13vPnC intramuscularly on Day 1.	

Serious adverse events	13vPnC: 6 to <18 Years	13vPnC: 18 to <65 Years	13vPnC: All Subjects
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 53 (0.00%)	0 / 153 (0.00%)	0 / 206 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	13vPnC: 6 to <18 Years	13vPnC: 18 to <65 Years	13vPnC: All Subjects
Total subjects affected by non-serious adverse events			
subjects affected / exposed	49 / 53 (92.45%)	121 / 153 (79.08%)	170 / 206 (82.52%)
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 53 (0.00%)	1 / 153 (0.65%)	1 / 206 (0.49%)
occurrences (all)	0	1	1
Wrist fracture			

subjects affected / exposed	0 / 53 (0.00%)	1 / 153 (0.65%)	1 / 206 (0.49%)
occurrences (all)	0	1	1
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 53 (0.00%)	1 / 153 (0.65%)	1 / 206 (0.49%)
occurrences (all)	0	1	1
Headache	Additional description: Number of subjects exposed = number of subjects evaluable for the adverse event.		
alternative assessment type: Systematic			
subjects affected / exposed[1]	12 / 49 (24.49%)	33 / 141 (23.40%)	45 / 190 (23.68%)
occurrences (all)	12	33	45
General disorders and administration site conditions			
Fatigue	Additional description: Number of subjects exposed = number of subjects evaluable for the adverse event.		
alternative assessment type: Systematic			
subjects affected / exposed[2]	18 / 48 (37.50%)	47 / 142 (33.10%)	65 / 190 (34.21%)
occurrences (all)	18	47	65
Redness	Additional description: Number of subjects exposed = number of subjects evaluable for the adverse event.		
alternative assessment type: Systematic			
subjects affected / exposed[3]	10 / 47 (21.28%)	10 / 135 (7.41%)	20 / 182 (10.99%)
occurrences (all)	10	10	20
Injection site erythema			
subjects affected / exposed	1 / 53 (1.89%)	0 / 153 (0.00%)	1 / 206 (0.49%)
occurrences (all)	1	0	1
Pain at the injection site	Additional description: Number of subjects exposed = number of subjects evaluable for the adverse event.		
alternative assessment type: Systematic			
subjects affected / exposed[4]	41 / 52 (78.85%)	96 / 145 (66.21%)	137 / 197 (69.54%)
occurrences (all)	41	96	137
Pyrexia	Additional description: Number of subjects exposed = number of subjects evaluable for the adverse event.		
alternative assessment type: Systematic			
subjects affected / exposed[5]	7 / 48 (14.58%)	8 / 134 (5.97%)	15 / 182 (8.24%)
occurrences (all)	7	8	15
Injection site swelling	Additional description: Number of subjects exposed = number of subjects evaluable for the adverse event.		
alternative assessment type: Systematic			

subjects affected / exposed[6]	16 / 47 (34.04%)	17 / 136 (12.50%)	33 / 183 (18.03%)
occurrences (all)	16	17	33
Injection site pain			
subjects affected / exposed	1 / 53 (1.89%)	2 / 153 (1.31%)	3 / 206 (1.46%)
occurrences (all)	1	2	3
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	0 / 53 (0.00%)	1 / 153 (0.65%)	1 / 206 (0.49%)
occurrences (all)	0	1	1
Gastrointestinal disorders			
Diarrhoea	Additional description: Number of subjects exposed = number of subjects evaluable for the adverse event.		
alternative assessment type: Systematic			
subjects affected / exposed[7]	4 / 48 (8.33%)	26 / 141 (18.44%)	30 / 189 (15.87%)
occurrences (all)	4	26	30
Vomiting	Additional description: Number of subjects exposed = number of subjects evaluable for the adverse event.		
alternative assessment type: Systematic			
subjects affected / exposed[8]	0 / 47 (0.00%)	2 / 136 (1.47%)	2 / 183 (1.09%)
occurrences (all)	0	2	2
Enteritis			
subjects affected / exposed	1 / 53 (1.89%)	0 / 153 (0.00%)	1 / 206 (0.49%)
occurrences (all)	1	0	1
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 53 (1.89%)	0 / 153 (0.00%)	1 / 206 (0.49%)
occurrences (all)	1	0	1
Hyperventilation			
subjects affected / exposed	0 / 53 (0.00%)	1 / 153 (0.65%)	1 / 206 (0.49%)
occurrences (all)	0	1	1
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 53 (0.00%)	1 / 153 (0.65%)	1 / 206 (0.49%)
occurrences (all)	0	1	1
Rash papular			
subjects affected / exposed	1 / 53 (1.89%)	0 / 153 (0.00%)	1 / 206 (0.49%)
occurrences (all)	1	0	1
Psychiatric disorders			

Middle insomnia			
subjects affected / exposed	0 / 53 (0.00%)	1 / 153 (0.65%)	1 / 206 (0.49%)
occurrences (all)	0	1	1
Musculoskeletal and connective tissue disorders			
Arthralgia	Additional description: Number of subjects exposed = number of subjects evaluable for the adverse event.		
alternative assessment type: Systematic			
subjects affected / exposed[9]	3 / 48 (6.25%)	19 / 138 (13.77%)	22 / 186 (11.83%)
occurrences (all)	3	19	22
Back pain			
subjects affected / exposed	0 / 53 (0.00%)	1 / 153 (0.65%)	1 / 206 (0.49%)
occurrences (all)	0	1	1
Myalgia	Additional description: Number of subjects exposed = number of subjects evaluable for the adverse event.		
alternative assessment type: Systematic			
subjects affected / exposed[10]	15 / 49 (30.61%)	38 / 139 (27.34%)	53 / 188 (28.19%)
occurrences (all)	15	38	53
Pain in extremity			
subjects affected / exposed	0 / 53 (0.00%)	1 / 153 (0.65%)	1 / 206 (0.49%)
occurrences (all)	0	1	1
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	0 / 53 (0.00%)	1 / 153 (0.65%)	1 / 206 (0.49%)
occurrences (all)	0	1	1
Bronchitis			
subjects affected / exposed	0 / 53 (0.00%)	1 / 153 (0.65%)	1 / 206 (0.49%)
occurrences (all)	0	1	1
Gastroenteritis			
subjects affected / exposed	0 / 53 (0.00%)	1 / 153 (0.65%)	1 / 206 (0.49%)
occurrences (all)	0	1	1
Herpes zoster			
subjects affected / exposed	0 / 53 (0.00%)	1 / 153 (0.65%)	1 / 206 (0.49%)
occurrences (all)	0	1	1
Nasopharyngitis			
subjects affected / exposed	1 / 53 (1.89%)	8 / 153 (5.23%)	9 / 206 (4.37%)
occurrences (all)	1	8	9
Pharyngitis			

subjects affected / exposed	3 / 53 (5.66%)	2 / 153 (1.31%)	5 / 206 (2.43%)
occurrences (all)	3	2	5
Upper respiratory tract infection			
subjects affected / exposed	0 / 53 (0.00%)	1 / 153 (0.65%)	1 / 206 (0.49%)
occurrences (all)	0	1	1
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 53 (1.89%)	0 / 153 (0.00%)	1 / 206 (0.49%)
occurrences (all)	1	0	1

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The number of subjects evaluable for this particular adverse event was 49, 141 and 190 for reporting arms "13vPnC: 6 to <18 Years", "13vPnC: 18 to <65 Years" and ''13vPnC: All Subjects'' respectively.

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The number of subjects evaluable for this particular adverse event was 48, 142 and 190 for reporting arms "13vPnC: 6 to <18 Years", "13vPnC: 18 to <65 Years" and ''13vPnC: All Subjects'' respectively.

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The number of subjects evaluable for this particular adverse event was 47, 135 and 182 for reporting arms "13vPnC: 6 to <18 Years", "13vPnC: 18 to <65 Years" and ''13vPnC: All Subjects'' respectively.

[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The number of subjects evaluable for this particular adverse event was 52, 145 and 197 for reporting arms "13vPnC: 6 to <18 Years", "13vPnC: 18 to <65 Years" and ''13vPnC: All Subjects'' respectively.

[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The number of subjects evaluable for this particular adverse event was 48, 134 and 182 for reporting arms "13vPnC: 6 to <18 Years", "13vPnC: 18 to <65 Years" and ''13vPnC: All Subjects'' respectively.

[6] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The number of subjects evaluable for this particular adverse event was 47, 136 and 183 for reporting arms "13vPnC: 6 to <18 Years", "13vPnC: 18 to <65 Years" and ''13vPnC: All Subjects'' respectively.

[7] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The number of subjects evaluable for this particular adverse event was 48, 141 and 189 for reporting arms "13vPnC: 6 to <18 Years", "13vPnC: 18 to <65 Years" and ''13vPnC: All Subjects'' respectively.

[8] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The number of subjects evaluable for this particular adverse event was 47, 136 and 183 for reporting arms "13vPnC: 6 to <18 Years", "13vPnC: 18 to <65 Years" and ''13vPnC: All Subjects'' respectively.

[9] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The number of subjects evaluable for this particular adverse event was 48, 138 and 186 for reporting arms "13vPnC: 6 to <18 Years", "13vPnC: 18 to <65 Years" and ''13vPnC: All Subjects'' respectively.

[10] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The number of subjects evaluable for this particular adverse event was 49, 139 and 188

for reporting arms “13vPnC: 6 to <18 Years”, “13vPnC: 18 to <65 Years” and ‘’13vPnC: All Subjects’’ respectively.

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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

OPA will be reported once available.

Notes: