Clinical trial results:
A Phase 2, Randomized, Open-Label Trial to Evaluate the Safety and Immunogenicity of a Multivalent Pneumococcal Conjugate Vaccine Given With, or Separately From, 13-valent Pneumococcal Conjugate Vaccine in Healthy Infants

Summary

EudraCT number	2020-005039-59
Trial protocol	Outside EU/EEA
Global end of trial date	05 November 2020

Results information

Result version number	v1 (current)
This version publication date	19 May 2021
First version publication date	19 May 2021

Trial information

Trial identification

Sponsor protocol code	C3571002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
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 18007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 18007181021, ClinicalTrials.gov_Inquiries@pfizer.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	23 March 2021

Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	05 November 2020
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To describe the safety profile of c7vPnC in healthy infants

Protection of trial subjects:

The study was conducted in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Council for Harmonization (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	01 June 2018
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	6 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 484
Worldwide total number of subjects	484
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)	484
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 565 subjects were randomized in 3 reporting groups– 512 subjects from 39 sites and 53 from 2 terminated sites (terminated due to serious quality issues). Study includes and reports valid data only from 512 subjects. Out of these 512 subjects, 484 received at least 1 vaccination.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1: c7vPnC and Prevenar 13 Co-administration

Arm description:

Subjects who received a dose of c7vPnC in one leg and Prevenar 13 and other vaccines in the other leg at 2, 4, 6, and 12 months of age (Dose 1, 2, 3, and 4 respectively).

Arm type	Experimental
Investigational medicinal product name	c7vPnC and Prevenar 13
Investigational medicinal product code	c7vPnC, Prevenar 13
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received c7vPnC 0.5 mL IM and Prevenar 13 IM.

Arm title	Group 2: c7vPnC and Prevenar 13 Staggered Administration

Arm description:

Subjects who received a dose of c7vPnC at 3, 5, 7, and 13 months of age in one leg (Dose 1, 2, 3, and 4 respectively) and Prevenar 13 in the other leg at 2, 4, 6, and 12 month of age.

Arm type	Experimental
Investigational medicinal product name	c7vPnC and Prevenar 13
Investigational medicinal product code	c7vPnC, Prevenar 13
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received c7vPnC 0.5 mL IM and Prevenar 13 IM.

Arm title	Group 3: Prevenar 13 as Control With Supplemental c7vPnC Dose

Arm description:

Subjects who received a dose of Prevenar 13 at 2, 4, 6, and 12 months of age (Dose 1, 2, 3, and 4 respectively) and a dose of c7vPnC at 13 months (Supplemental Dose).

Arm type	Experimental

Investigational medicinal product name	c7vPnC and Prevenar 13
Investigational medicinal product code	c7vPnC and Prevenar 13
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received supplemental dose of c7vPnC and Prevenar 13 IM.

Number of subjects in period 1	Group 1: c7vPnC and Prevenar 13 Co-administration	Group 2: c7vPnC and Prevenar 13 Staggered Administration	Group 3: Prevenar 13 as Control With Supplemental c7vPnC Dose
Started	171	147	166
Completed	95	77	72
Not completed	76	70	94
Withdrawal by parent/guardian	20	18	26
No longer meets eligibility criteria	3	5	6
Study terminated by sponsor	44	37	48
Adverse event, non-fatal	-	1	-
Unspecified	4	2	2
Lost to follow-up	5	7	12

Baseline characteristics

Reporting groups	
Reporting group title	Group 1: c7vPnC and Prevenar 13 Co-administration
Reporting group description:	
Subjects who received a dose of c7vPnC in one leg and Prevenar 13 and other vaccines in the other leg at 2, 4, 6, and 12 months of age (Dose 1, 2, 3, and 4 respectively).	
Reporting group title	Group 2: c7vPnC and Prevenar 13 Staggered Administration
Reporting group description:	
Subjects who received a dose of c7vPnC at 3, 5, 7, and 13 months of age in one leg (Dose 1, 2, 3, and 4 respectively) and Prevenar 13 in the other leg at 2, 4, 6, and 12 month of age.	
Reporting group title	Group 3: Prevenar 13 as Control With Supplemental c7vPnC Dose
Reporting group description:	
Subjects who received a dose of Prevenar 13 at 2, 4, 6, and 12 months of age (Dose 1, 2, 3, and 4 respectively) and a dose of c7vPnC at 13 months (Supplemental Dose).	

Reporting group values	Group 1: c7vPnC and Prevenar 13 Co-administration	Group 2: c7vPnC and Prevenar 13 Staggered Administration	Group 3: Prevenar 13 as Control With Supplemental c7vPnC Dose
Number of subjects	171	147	166
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)	171	147	166
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: Years			
arithmetic mean	65.9	95.1	64.9
standard deviation	± 9.53	± 10.40	± 8.22
Sex: Female, Male Units: Subjects			
Female	85	80	75
Male	86	67	91
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	4	8	3
Asian	7	5	3
Native Hawaiian or Other Pacific Islander	0	0	1
Black or African American	35	26	31
White	102	90	105
More than one race	6	4	6

Unknown or Not Reported	17	14	17
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	89	70	85
Not Hispanic or Latino	81	77	80
Unknown or Not Reported	1	0	1

Reporting group values	Total		
Number of subjects	484		
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)	484		
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: Years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male Units: Subjects			
Female	240		
Male	244		
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	15		
Asian	15		
Native Hawaiian or Other Pacific Islander	1		
Black or African American	92		
White	297		
More than one race	16		
Unknown or Not Reported	48		
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	244		
Not Hispanic or Latino	238		
Unknown or Not Reported	2		

End points

End points reporting groups

Reporting group title	Group 1: c7vPnC and Prevenar 13 Co-administration
Reporting group description:	
Subjects who received a dose of c7vPnC in one leg and Prevenar 13 and other vaccines in the other leg at 2, 4, 6, and 12 months of age (Dose 1, 2, 3, and 4 respectively).	
Reporting group title	Group 2: c7vPnC and Prevenar 13 Staggered Administration
Reporting group description:	
Subjects who received a dose of c7vPnC at 3, 5, 7, and 13 months of age in one leg (Dose 1, 2, 3, and 4 respectively) and Prevenar 13 in the other leg at 2, 4, 6, and 12 month of age.	
Reporting group title	Group 3: Prevenar 13 as Control With Supplemental c7vPnC Dose
Reporting group description:	
Subjects who received a dose of Prevenar 13 at 2, 4, 6, and 12 months of age (Dose 1, 2, 3, and 4 respectively) and a dose of c7vPnC at 13 months (Supplemental Dose).	

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

End point title	Percentage of Subjects With Local Reactions Within 7 Days After Dose 1[1]
End point description:	
Local reactions were recorded using an electronic diary by subject's legally acceptable representative (LAR). Local reactions included redness, swelling and pain at the injection site. Redness and swelling were measured and recorded in measuring device units. 1 measuring device unit =0.5 centimeter (cm). Redness and swelling were graded as mild (0.5 to 2.0 cm), moderate (>2.0 to 7.0 cm) and severe (>7 cm). Pain at injection site was graded as mild (hurt if gently touched), moderate (hurt if gently touched, with crying), and severe (caused limitation of limb movement). The overall safety population included all subjects who received at least 1 dose of c7vPnC (in Groups 1 and 2) or Prevenar 13 (in Group 3) and had safety data reported in the study. Here, "Number of Subjects Analysed" signifies number of subjects with any e-diary data reported after Dose 1 in the overall safety population. Dose 1 was first dose of c7vPnC in Group 1 and Groups 2, and first dose of Prevenar 13 in Group 3.	
End point type	Primary
End point timeframe:	
Within 7 Days After Dose 1	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analysed for this endpoint

End point values	Group 1: c7vPnC and Prevenar 13 Co-administration	Group 2: c7vPnC and Prevenar 13 Staggered Administration	Group 3: Prevenar 13 as Control With Supplemental c7vPnC Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	166	144	165	
Units: Percentage of Subjects				
number (confidence interval 95%)				
Redness: Any	25.9 (19.4 to 33.3)	26.4 (19.4 to 34.4)	21.8 (15.8 to 28.9)	
Redness: Mild	16.3 (11.0 to 22.8)	21.5 (15.1 to 29.1)	18.2 (12.6 to 24.9)	
Redness: Moderate	9.6 (5.6 to 15.2)	4.9 (2.0 to 9.8)	3.6 (1.3 to 7.7)	
Redness: Severe	0 (0.0 to 2.2)	0 (0.0 to 2.5)	0 (0.0 to 2.2)	

Swelling: Any	27.1 (20.5 to 34.5)	22.2 (15.7 to 29.9)	23.6 (17.4 to 30.9)	
Swelling: Mild	16.3 (11.0 to 22.8)	13.9 (8.7 to 20.6)	17.0 (11.6 to 23.6)	
Swelling: Moderate	10.2 (6.1 to 15.9)	8.3 (4.4 to 14.1)	5.5 (2.5 to 10.1)	
Swelling: Severe	0.6 (0.0 to 3.3)	0 (0.0 to 2.5)	1.2 (0.1 to 4.3)	
Pain at Injection Site: Any	59.6 (51.8 to 67.2)	40.3 (32.2 to 48.8)	50.3 (42.4 to 58.2)	
Pain at Injection Site: Mild	28.9 (22.2 to 36.4)	28.5 (21.3 to 36.6)	26.1 (19.5 to 33.5)	
Pain at Injection Site: Moderate	27.7 (21.1 to 35.2)	11.1 (6.5 to 17.4)	22.4 (16.3 to 29.6)	
Pain at Injection Site: Severe	3.0 (1.0 to 6.9)	0.7 (0.0 to 3.8)	1.8 (0.4 to 5.2)	

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Local reactions were recorded using an electronic diary by subject's LAR. Local reactions included redness, swelling and pain at the injection site. Redness and swelling were measured and recorded in measuring device units. 1 measuring device unit =0.5 cm. Redness and swelling were graded as mild (0.5 to 2.0 cm), moderate (>2.0 to 7.0 cm) and severe (>7 cm). Pain at injection site was graded as mild (hurt if gently touched), moderate (hurt if gently touched, with crying), and severe (caused limitation of limb movement).The overall safety population included all subjects who received at least 1 dose of c7vPnC (in Groups 1 and 2) or Prevenar 13 (in Group 3) and had safety data reported in the study. Here, "Number of Subjects Analysed" signifies number of subjects with any e-diary data reported after Dose 2 in the overall safety population. Dose 2 was second dose of c7vPnC in Group 1 and Groups 2, and second dose of Prevenar 13 in Group 3.

End point type	Primary

End point timeframe:

Within 7 Days After Dose 2

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analysed for this endpoint

End point values	Group 1: c7vPnC and Prevenar 13 Co-administration	Group 2: c7vPnC and Prevenar 13 Staggered Administration	Group 3: Prevenar 13 as Control With Supplemental c7vPnC Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	152	126	147	
Units: Percentage of Subjects				
number (confidence interval 95%)				
Redness: Any	28.9 (21.9 to 36.8)	20.6 (13.9 to 28.8)	23.8 (17.2 to 31.5)	
Redness: Mild	22.4 (16.0 to 29.8)	18.3 (11.9 to 26.1)	21.1 (14.8 to 28.6)	
Redness: Moderate	6.6 (3.2 to 11.8)	2.4 (0.5 to 6.8)	2.7 (0.7 to 6.8)	

Redness: Severe	0 (0.0 to 2.4)	0 (0.0 to 2.9)	0 (0.0 to 2.5)	
Swelling: Any	21.1 (14.9 to 28.4)	16.7 (10.6 to 24.3)	22.4 (16.0 to 30.1)	
Swelling: Mild	14.5 (9.3 to 21.1)	14.3 (8.7 to 21.6)	16.3 (10.7 to 23.3)	
Swelling: Moderate	6.6 (3.2 to 11.8)	2.4 (0.5 to 6.8)	6.1 (2.8 to 11.3)	
Swelling: Severe	0 (0.0 to 2.4)	0 (0.0 to 2.9)	0 (0.0 to 2.5)	
Pain at Injection Site: Any	55.3 (47.0 to 63.3)	23.8 (16.7 to 32.2)	46.9 (38.7 to 55.3)	
Pain at Injection Site: Mild	31.6 (24.3 to 39.6)	19.0 (12.6 to 27.0)	27.9 (20.8 to 35.9)	
Pain at Injection Site: Moderate	21.7 (15.4 to 29.1)	4.8 (1.8 to 10.1)	18.4 (12.5 to 25.6)	
Pain at Injection Site: Severe	2.0 (0.4 to 5.7)	0 (0.0 to 2.9)	0.7 (0.0 to 3.7)	

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Local reactions were recorded using an electronic diary by subject's LAR. Local reactions included redness, swelling and pain at the injection site. Redness and swelling were measured and recorded in measuring device units. 1 measuring device unit =0.5 cm. Redness and swelling were graded as mild (0.5 to 2.0 cm), moderate (>2.0 to 7.0 cm) and severe (>7 cm). Pain at injection site was graded as mild (hurt if gently touched), moderate (hurt if gently touched, with crying), and severe (caused limitation of limb movement). The overall safety population included all subjects who received at least 1 dose of c7vPnC (in Groups 1 and 2) or Prevenar 13 (in Group 3) and had safety data reported in the study. Here, "Number of Subjects Analysed" signifies number of subjects with any e-diary data reported after Dose 3 in the overall safety population. Dose 3 was third dose of c7vPnC in Group 1 and Groups 2, and third dose of Prevenar 13 in Group 3.

End point type	Primary

End point timeframe:

Within 7 Days After Dose 3

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analysed for this endpoint

End point values	Group 1: c7vPnC and Prevenar 13 Co-administration	Group 2: c7vPnC and Prevenar 13 Staggered Administration	Group 3: Prevenar 13 as Control With Supplemental c7vPnC Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	143	120	138	
Units: Percentage of Subjects				
number (confidence interval 95%)				
Redness: Any	25.2 (18.3 to 33.1)	20.0 (13.3 to 28.3)	22.5 (15.8 to 30.3)	
Redness: Mild	23.1 (16.4 to 30.9)	19.2 (12.6 to 27.4)	18.1 (12.1 to 25.6)	
Redness: Moderate	2.1 (0.4 to 6.0)	0.8 (0.0 to 4.6)	4.3 (1.6 to 9.2)	

Redness: Severe	0 (0.0 to 2.5)	0 (0.0 to 3.0)	0 (0.0 to 2.6)	
Swelling: Any	21.7 (15.2 to 29.3)	14.2 (8.5 to 21.7)	18.1 (12.1 to 25.6)	
Swelling: Mild	17.5 (11.6 to 24.7)	11.7 (6.5 to 18.8)	13.8 (8.5 to 20.7)	
Swelling: Moderate	4.2 (1.6 to 8.9)	2.5 (0.5 to 7.1)	3.6 (1.2 to 8.3)	
Swelling: Severe	0 (0.0 to 2.5)	0 (0.0 to 3.0)	0.7 (0.0 to 4.0)	
Pain at Injection Site: Any	39.9 (31.8 to 48.4)	22.5 (15.4 to 31.0)	35.5 (27.6 to 44.1)	
Pain at Injection Site: Mild	23.8 (17.1 to 31.6)	17.5 (11.2 to 25.5)	18.8 (12.7 to 26.4)	
Pain at Injection Site: Moderate	15.4 (9.9 to 22.4)	5.0 (1.9 to 10.6)	15.2 (9.7 to 22.3)	
Pain at Injection Site: Severe	0.7 (0.0 to 3.8)	0 (0.0 to 3.0)	1.4 (0.2 to 5.1)	

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Local reactions were recorded using an electronic diary by subject's LAR. Local reactions included redness, swelling and pain at the injection site. Redness and swelling were measured and recorded in measuring device units. 1 measuring device unit =0.5 cm. Redness and swelling were graded as mild (0.5 to 2.0 cm), moderate (>2.0 to 7.0 cm) and severe (>7 cm). Pain at injection site was graded as mild (hurt if gently touched), moderate (hurt if gently touched, with crying), and severe (caused limitation of limb movement). Dose 4 safety analysis set included subjects who received Dose 4 and had safety data between Dose 4 and 1 month after Dose 4 for Groups 1 and 2 and had safety data between Dose 4 and Supplemental Dose for Group 3. Here, "Number of Subjects Analysed" signifies number of subjects with any e-diary data reported after Dose 4 in the Dose 4 safety analysis set. Dose 4 was the fourth dose of c7vPnC in Group 1 and Groups 2, and fourth dose of Prevenar 13 in Group 3.

End point type	Primary

End point timeframe:

Within 7 Days After Dose 4

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analysed for this endpoint

End point values	Group 1: c7vPnC and Prevenar 13 Co-administration	Group 2: c7vPnC and Prevenar 13 Staggered Administration	Group 3: Prevenar 13 as Control With Supplemental c7vPnC Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	105	79	98	
Units: Percentage of Subjects				
number (confidence interval 95%)				
Redness: Any	22.9 (15.2 to 32.1)	19.0 (11.0 to 29.4)	22.4 (14.6 to 32.0)	
Redness: Mild	21.9 (14.4 to 31.0)	15.2 (8.1 to 25.0)	19.4 (12.1 to 28.6)	
Redness: Moderate	1.0 (0.0 to 5.2)	3.8 (0.8 to 10.7)	3.1 (0.6 to 8.7)	

Redness: Severe	0 (0.0 to 3.5)	0 (0.0 to 4.6)	0 (0.0 to 3.7)	
Swelling: Any	19.0 (12.0 to 27.9)	13.9 (7.2 to 23.5)	19.4 (12.1 to 28.6)	
Swelling: Mild	17.1 (10.5 to 25.7)	8.9 (3.6 to 17.4)	13.3 (7.3 to 21.6)	
Swelling: Moderate	1.9 (0.2 to 6.7)	5.1 (1.4 to 12.5)	6.1 (2.3 to 12.9)	
Swelling: Severe	0 (0.0 to 3.5)	0 (0.0 to 4.6)	0 (0.0 to 3.7)	
Pain at Injection Site: Any	35.2 (26.2 to 45.2)	22.8 (14.1 to 33.6)	28.6 (19.9 to 38.6)	
Pain at Injection Site: Mild	21.9 (14.4 to 31.0)	16.5 (9.1 to 26.5)	18.4 (11.3 to 27.5)	
Pain at Injection Site: Moderate	12.4 (6.8 to 20.2)	6.3 (2.1 to 14.2)	10.2 (5.0 to 18.0)	
Pain at Injection Site: Severe	1.0 (0.0 to 5.2)	0 (0.0 to 4.6)	0 (0.0 to 3.7)	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Local Reactions (LR) Within 7 Days After Supplemental Dose

End point title	Percentage of Subjects With Local Reactions (LR) Within 7 Days After Supplemental Dose[5][6]

End point description:

Supplemental dose safety analysis set included subjects who received Supplemental Dose and had safety data between Supplemental Dose and 1 month after Supplemental Dose. Data in this endpoint was planned to be collected and analysed only for Prevenar 13 as Control with supplemental c7vPnC dose arm (Group 3) and not planned to be collected and analysed for c7vPnC and Prevenar 13 Co-administration (Group 1) and c7vPnC and Prevenar 13 Staggered Administration (Group 2), as pre-specified in protocol. Number of Subjects Analysed = number of subjects with e-diary data reported after vaccination in supplemental dose safety population.

End point type	Primary

End point timeframe:

Within 7 Days After Supplemental Dose

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analysed 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 analyzed only for the reporting arm specified

End point values	Group 3: Prevenar 13 as Control With Supplemental c7vPnC Dose			
Subject group type	Reporting group			
Number of subjects analysed	85			
Units: Percentage of Subjects				
number (confidence interval 95%)				
Redness: Any	5.9 (1.9 to 13.2)			
Redness: Mild	4.7 (1.3 to 11.6)			

Redness: Moderate	1.2 (0.0 to 6.4)			
Redness: Severe	0 (0.0 to 4.2)			
Swelling: Any	9.4 (4.2 to 17.7)			
Swelling: Mild	9.4 (4.2 to 17.7)			
Swelling: Moderate	0 (0.0 to 4.2)			
Swelling: Severe	0 (0.0 to 4.2)			
Pain at Injection Site: Any	12.9 (6.6 to 22.0)			
Pain at Injection Site: Mild	11.8 (5.8 to 20.6)			
Pain at Injection Site: Moderate	1.2 (0.0 to 6.4)			
Pain at Injection Site: Severe	0 (0.0 to 4.2)			

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

SE:using an e-diary by subject's LAR and included fever, decreased appetite, drowsiness/increased sleep, and irritability.Fever:as rectal temperature of >=38.0 degree(deg) Celsius (C) and categorized to >=38.0 to 38.4 deg C, >38.4 to 38.9 deg C, >38.9 to 40.0 deg C and >40.0 deg C. Decreased appetite: graded as mild (decreased interest in eating), moderate (decreased oral intake) and severe (refusal to feed). Drowsiness: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). Overall safety set analysed.Number of Subjects Analysed=number of subjects with any e-diary data reported after Dose 1 in overall safety population.Dose 1 was first dose of c7vPnC in Group 1 and Groups 2, and first dose of Prevenar 13 in Group 3.

End point type	Primary

End point timeframe:

Within 7 Days After Dose 1

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analysed for this endpoint

End point values	Group 1: c7vPnC and Prevenar 13 Co-administration	Group 2: c7vPnC and Prevenar 13 Staggered Administration	Group 3: Prevenar 13 as Control With Supplemental c7vPnC Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	166	144	165	
Units: Percentage of Subjects				
number (confidence interval 95%)				
Fever: >=38.0 degree C	12.7 (8.0 to 18.7)	5.6 (2.4 to 10.7)	9.1 (5.2 to 14.6)	
Fever: >=38.0 degree C to 38.4 degree C	7.8 (4.2 to 13.0)	3.5 (1.1 to 7.9)	6.1 (2.9 to 10.9)	
Fever: >38.4 degree C to 38.9 degree C	3.0 (1.0 to 6.9)	0.7 (0.0 to 3.8)	2.4 (0.7 to 6.1)	

Fever: >38.9 degree C to 40.0 degree C	1.8 (0.4 to 5.2)	1.4 (0.2 to 4.9)	0.6 (0.0 to 3.3)	
Fever: >40.0 degree C	0 (0.0 to 2.2)	0 (0.0 to 2.5)	0 (0.0 to 2.2)	
Decreased Appetite: Any	28.9 (22.2 to 36.4)	15.3 (9.8 to 22.2)	26.7 (20.1 to 34.1)	
Decreased Appetite: Mild	19.3 (13.6 to 26.1)	6.3 (2.9 to 11.5)	14.5 (9.5 to 20.9)	
Decreased Appetite: Moderate	7.2 (3.8 to 12.3)	9.0 (4.9 to 14.9)	10.3 (6.1 to 16.0)	
Decreased Appetite: Severe	2.4 (0.7 to 6.1)	0 (0.0 to 2.5)	1.8 (0.4 to 5.2)	
Drowsiness: Any	59.6 (51.8 to 67.2)	43.1 (34.8 to 51.6)	53.3 (45.4 to 61.1)	
Drowsiness: Mild	41.6 (34.0 to 49.5)	31.9 (24.4 to 40.2)	38.2 (30.7 to 46.1)	
Drowsiness: Moderate	16.3 (11.0 to 22.8)	9.7 (5.4 to 15.8)	13.3 (8.5 to 19.5)	
Drowsiness: Severe	1.8 (0.4 to 5.2)	1.4 (0.2 to 4.9)	1.8 (0.4 to 5.2)	
Irritability: Any	70.5 (62.9 to 77.3)	57.6 (49.1 to 65.8)	63.6 (55.8 to 71.0)	
Irritability: Mild	25.3 (18.9 to 32.6)	29.2 (21.9 to 37.3)	23.6 (17.4 to 30.9)	
Irritability: Moderate	38.0 (30.5 to 45.8)	23.6 (16.9 to 31.4)	36.4 (29.0 to 44.2)	
Irritability: Severe	7.2 (3.8 to 12.3)	4.9 (2.0 to 9.8)	3.6 (1.3 to 7.7)	

Statistical analyses

No statistical analyses for this end point

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

End point title	Percentage of Subjects With Systemic Events Within 7 Days After Dose 2[8]

End point description:

SE:using an e-diary by subject's LAR and included fever, decreased appetite, drowsiness/increased sleep, and irritability.Fever:as rectal temperature of >=38.0 degree(deg) Celsius (C) and categorized to >=38.0 to 38.4 deg C, >38.4 to 38.9 deg C, >38.9 to 40.0 deg C and >40.0 degC. Decreased appetite: graded as mild (decreased interest in eating), moderate (decreased oral intake) and severe (refusal to feed). Drowsiness: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). Overall safety set analysed.Number of Subjects Analysed=number of subjects with any e-diary data reported after Dose 2 in overall safety population.Dose 2 was second dose of c7vPnC in Group 1 and Groups 2, and second dose of Prevenar 13 in Group 3.

End point type	Primary

End point timeframe:

Within 7 Days After Dose 2

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analysed for this endpoint

End point values	Group 1: c7vPnC and Prevenar 13 Co-administration	Group 2: c7vPnC and Prevenar 13 Staggered Administration	Group 3: Prevenar 13 as Control With Supplemental c7vPnC Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	152	126	147	
Units: Percentage of Subjects				
number (confidence interval 95%)				
Fever: >=38.0 degree C	25.7 (18.9 to 33.4)	4.0 (1.3 to 9.0)	15.6 (10.2 to 22.5)	
Fever: >=38.0 degree C to 38.4 degree C	12.5 (7.7 to 18.8)	3.2 (0.9 to 7.9)	8.2 (4.3 to 13.8)	
Fever: >38.4 degree C to 38.9 degree C	10.5 (6.1 to 16.5)	0.8 (0.0 to 4.3)	2.7 (0.7 to 6.8)	
Fever: >38.9 degree C to 40.0 degree C	2.6 (0.7 to 6.6)	0 (0.0 to 2.9)	4.1 (1.5 to 8.7)	
Fever: >40.0 degree C	0 (0.0 to 2.4)	0 (0.0 to 2.9)	0.7 (0.0 to 3.7)	
Decreased Appetite: Any	23.0 (16.6 to 30.5)	12.7 (7.4 to 19.8)	25.2 (18.4 to 33.0)	
Decreased Appetite: Mild	11.8 (7.2 to 18.1)	8.7 (4.4 to 15.1)	15.6 (10.2 to 22.5)	
Decreased Appetite: Moderate	9.9 (5.6 to 15.8)	4.0 (1.3 to 9.0)	9.5 (5.3 to 15.5)	
Decreased Appetite: Severe	1.3 (0.2 to 4.7)	0 (0.0 to 2.9)	0 (0.0 to 2.5)	
Drowsiness: Any	48.7 (40.5 to 56.9)	21.4 (14.6 to 29.6)	42.9 (34.7 to 51.3)	
Drowsiness: Mild	32.2 (24.9 to 40.3)	15.1 (9.3 to 22.5)	25.9 (19.0 to 33.7)	
Drowsiness: Moderate	15.1 (9.8 to 21.8)	6.3 (2.8 to 12.1)	17.0 (11.3 to 24.1)	
Drowsiness: Severe	1.3 (0.2 to 4.7)	0 (0.0 to 2.9)	0 (0.0 to 2.5)	
Irritability: Any	64.5 (56.3 to 72.1)	44.4 (35.6 to 53.6)	58.5 (50.1 to 66.6)	
Irritability: Mild	20.4 (14.3 to 27.7)	21.4 (14.6 to 29.6)	17.7 (11.9 to 24.8)	
Irritability: Moderate	40.8 (32.9 to 49.0)	20.6 (13.9 to 28.8)	36.1 (28.3 to 44.4)	
Irritability: Severe	3.3 (1.1 to 7.5)	2.4 (0.5 to 6.8)	4.8 (1.9 to 9.6)	

Statistical analyses

No statistical analyses for this end point

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

End point title	Percentage of Subjects With Systemic Events Within 7 Days After Dose 3[9]

End point description:

SE:using an e-diary by subject's LAR and included fever, decreased appetite, drowsiness/increased sleep, and irritability.Fever:as rectal temperature of >=38.0 degree(deg) Celsius (C) and categorized to >=38.0 to 38.4 deg C, >38.4 to 38.9 deg C, >38.9 to 40.0 deg C and >40.0 deg C. Decreased appetite: graded as mild (decreased interest in eating), moderate (decreased oral intake) and severe (refusal to feed). Drowsiness: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). Overall safety set analysed.Number of Subjects Analysed=number of subjects with any e-diary data reported after Dose 3 in overall safety population.Dose 3 was third dose of c7vPnC in Group 1 and Groups 2, and third dose of Prevenar 13 in Group 3.

End point type	Primary

End point timeframe:

Within 7 Days After Dose 3

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analysed for this endpoint

End point values	Group 1: c7vPnC and Prevenar 13 Co-administration	Group 2: c7vPnC and Prevenar 13 Staggered Administration	Group 3: Prevenar 13 as Control With Supplemental c7vPnC Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	143	120	138	
Units: Percentage of Subjects				
number (confidence interval 95%)				
Fever: >=38.0 degree C	14.0 (8.8 to 20.8)	5.8 (2.4 to 11.6)	14.5 (9.1 to 21.5)	
Fever: >=38.0 degree C to 38.4 degree C	6.3 (2.9 to 11.6)	3.3 (0.9 to 8.3)	8.0 (4.0 to 13.8)	
Fever: >38.4 degree C to 38.9 degree C	5.6 (2.4 to 10.7)	1.7 (0.2 to 5.9)	2.9 (0.8 to 7.3)	
Fever: >38.9 degree C to 40.0 degree C	1.4 (0.2 to 5.0)	0.8 (0.0 to 4.6)	3.6 (1.2 to 8.3)	
Fever: >40.0 degree C	0.7 (0.0 to 3.8)	0 (0.0 to 3.0)	0 (0.0 to 2.6)	
Decreased Appetite: Any	19.6 (13.4 to 27.0)	18.3 (11.9 to 26.4)	21.0 (14.5 to 28.8)	
Decreased Appetite: Mild	12.6 (7.6 to 19.2)	12.5 (7.2 to 19.8)	10.1 (5.7 to 16.4)	
Decreased Appetite: Moderate	7.0 (3.4 to 12.5)	5.8 (2.4 to 11.6)	10.1 (5.7 to 16.4)	
Decreased Appetite: Severe	0 (0.0 to 2.5)	0 (0.0 to 3.0)	0.7 (0.0 to 4.0)	
Drowsiness: Any	43.4 (35.1 to 51.9)	21.7 (14.7 to 30.1)	45.7 (37.2 to 54.3)	
Drowsiness: Mild	29.4 (22.1 to 37.6)	16.7 (10.5 to 24.6)	32.6 (24.9 to 41.1)	
Drowsiness: Moderate	13.3 (8.2 to 20.0)	3.3 (0.9 to 8.3)	12.3 (7.3 to 19.0)	
Drowsiness: Severe	0.7 (0.0 to 3.8)	1.7 (0.2 to 5.9)	0.7 (0.0 to 4.0)	
Irritability: Any	57.3 (48.8 to 65.6)	50.8 (41.6 to 60.1)	53.6 (44.9 to 62.1)	
Irritability: Mild	25.2 (18.3 to 33.1)	26.7 (19.0 to 35.5)	23.9 (17.1 to 31.9)	
Irritability: Moderate	31.5 (24.0 to 39.8)	21.7 (14.7 to 30.1)	26.8 (19.6 to 35.0)	
Irritability: Severe	0.7 (0.0 to 3.8)	2.5 (0.5 to 7.1)	2.9 (0.8 to 7.3)	

Statistical analyses

No statistical analyses for this end point

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

End point title	Percentage of Subjects With Systemic Events Within 7 Days After Dose 4[10]

End point description:

SE:using an e-diary by subject's LAR and included fever, decreased appetite, drowsiness/increased sleep, and irritability. Fever: rectal temperature of >=38.0 deg C and categorized to >=38.0 to 38.4 deg C, >38.4 to 38.9 deg C, >38.9 to 40.0 deg C and >40.0 deg C. Decreased appetite: 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). Dose 4 safety analysis set analysed.Number of Subjects Analysed=number of subjects with any e-diary data reported after Dose 4 in Dose 4 safety analysis set. Dose 4 was fourth dose of c7vPnC in Group 1 and Groups 2, and fourth dose of Prevenar 13 in Group 3.

End point type	Primary

End point timeframe:

Within 7 Days After Dose 4

Notes:

[10] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analysed for this endpoint

End point values	Group 1: c7vPnC and Prevenar 13 Co-administration	Group 2: c7vPnC and Prevenar 13 Staggered Administration	Group 3: Prevenar 13 as Control With Supplemental c7vPnC Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	105	79	98	
Units: Percentage of Subjects				
number (confidence interval 95%)				
Fever: >=38.0 degree C	12.4 (6.8 to 20.2)	0 (0.0 to 4.6)	11.2 (5.7 to 19.2)	
Fever: >=38.0 degree C to 38.4 degree C	7.6 (3.3 to 14.5)	0 (0.0 to 4.6)	4.1 (1.1 to 10.1)	
Fever: >38.4 degree C to 38.9 degree C	1.9 (0.2 to 6.7)	0 (0.0 to 4.6)	4.1 (1.1 to 10.1)	
Fever: >38.9 degree C to 40.0 degree C	1.9 (0.2 to 6.7)	0 (0.0 to 4.6)	3.1 (0.6 to 8.7)	
Fever: >40.0 degree C	1.0 (0.0 to 5.2)	0 (0.0 to 4.6)	0 (0.0 to 3.7)	
Decreased Appetite: Any	20.0 (12.8 to 28.9)	13.9 (7.2 to 23.5)	23.5 (15.5 to 33.1)	
Decreased Appetite: Mild	14.3 (8.2 to 22.5)	10.1 (4.5 to 19.0)	13.3 (7.3 to 21.6)	
Decreased Appetite: Moderate	4.8 (1.6 to 10.8)	3.8 (0.8 to 10.7)	9.2 (4.3 to 16.7)	
Decreased Appetite: Severe	1.0 (0.0 to 5.2)	0 (0.0 to 4.6)	1.0 (0.0 to 5.6)	
Drowsiness: Any	33.3 (24.4 to 43.2)	20.3 (12.0 to 30.8)	29.6 (20.8 to 39.7)	
Drowsiness: Mild	25.7 (17.7 to 35.2)	17.7 (10.0 to 27.9)	20.4 (12.9 to 29.7)	
Drowsiness: Moderate	7.6 (3.3 to 14.5)	2.5 (0.3 to 8.8)	8.2 (3.6 to 15.5)	
Drowsiness: Severe	0 (0.0 to 3.5)	0 (0.0 to 4.6)	1.0 (0.0 to 5.6)	
Irritability: Any	60.0 (50.0 to 69.4)	53.2 (41.6 to 64.5)	46.9 (36.8 to 57.3)	
Irritability: Mild	24.8 (16.9 to 34.1)	31.6 (21.6 to 43.1)	21.4 (13.8 to 30.9)	
Irritability: Moderate	34.3 (25.3 to 44.2)	20.3 (12.0 to 30.8)	23.5 (15.5 to 33.1)	
Irritability: Severe	1.0 (0.0 to 5.2)	1.3 (0.0 to 6.9)	2.0 (0.2 to 7.2)	

Statistical analyses

No statistical analyses for this end point

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

End point title	Percentage of Subjects With Systemic Events Within 7 Days After Supplemental Dose[11][12]

End point description:

Supplemental dose safety analysis set included subjects who received Supplemental Dose and had safety data between Supplemental Dose and 1 month after Supplemental Dose. Data in this endpoint was planned to be collected and analysed only for Prevenar 13 as Control with supplemental c7vPnC dose arm (Group 3) and not planned to be collected and analysed for c7vPnC and Prevenar 13 Co-administration (Group 1) and c7vPnC and Prevenar 13 Staggered Administration (Group 2), as pre-specified in protocol. Number of Subjects Analysed = number of subjects with e-diary data reported after vaccination in supplemental dose safety population.

End point type	Primary

End point timeframe:

Within 7 Days After Supplemental Dose

Notes:

[11] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analysed for this endpoint

[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 analyzed only for the reporting arm specified

End point values	Group 3: Prevenar 13 as Control With Supplemental c7vPnC Dose			
Subject group type	Reporting group			
Number of subjects analysed	85			
Units: Percentage of Subjects				
number (confidence interval 95%)				
Fever: >=38.0 degree C	5.9 (1.9 to 13.2)			
Fever: >=38.0 degree C to 38.4 degree C	3.5 (0.7 to 10.0)			
Fever: >38.4 degree C to 38.9 degree C	1.2 (0.0 to 6.4)			
Fever: >38.9 degree C to 40.0 degree C	1.2 (0.0 to 6.4)			
Fever: >40.0 degree C	0 (0.0 to 4.2)			
Decreased Appetite: Any	11.8 (5.8 to 20.6)			
Decreased Appetite: Mild	8.2 (3.4 to 16.2)			
Decreased Appetite: Moderate	1.2 (0.0 to 6.4)			
Decreased Appetite: Severe	2.4 (0.3 to 8.2)			
Drowsiness: Any	21.2 (13.1 to 31.4)			
Drowsiness: Mild	17.6 (10.2 to 27.4)			
Drowsiness: Moderate	2.4 (0.3 to 8.2)			
Drowsiness: Severe	1.2 (0.0 to 6.4)			
Irritability: Any	30.6 (21.0 to 41.5)			

Irritability: Mild	15.3 (8.4 to 24.7)			
Irritability: Moderate	12.9 (6.6 to 22.0)			
Irritability: Severe	2.4 (0.3 to 8.2)			

Statistical analyses

No statistical analyses for this end point

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

End point title	Percentage of Subjects With Adverse Events (AEs) From Dose 1 to 1 Month After Dose 3[13]

End point description:

An AE was any untoward medical occurrence in study subjects who received study vaccine without regard to possibility of causal relationship with the treatment. The overall safety population included all subjects who received at least 1 dose of c7vPnC (in Groups 1 and 2) or Prevenar 13 (in Group 3) and had safety data reported in the study.

End point type	Primary

End point timeframe:

From Dose 1 to 1 Month After Dose 3 (up to 5 months)

Notes:

[13] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analysed for this endpoint

End point values	Group 1: c7vPnC and Prevenar 13 Co-administration	Group 2: c7vPnC and Prevenar 13 Staggered Administration	Group 3: Prevenar 13 as Control With Supplemental c7vPnC Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	171	147	166	
Units: Percentage of Subjects				
number (confidence interval 95%)	57.9 (50.1 to 65.4)	65.3 (57.0 to 73.0)	56.6 (48.7 to 64.3)	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Adverse Events (AEs) From Dose 4 to 1 Month After Dose 4

End point title	Percentage of Subjects With Adverse Events (AEs) From Dose 4 to 1 Month After Dose 4[14]

End point description:

An AE was any untoward medical occurrence in study subjects who received study vaccine without regard to possibility of causal relationship with the treatment. Dose 4 safety analysis set included subjects who received Dose 4 and had safety data between Dose 4 and 1 month after Dose 4 for Groups 1 and 2 and had safety data between Dose 4 and Supplemental Dose for Group 3.

End point type	Primary

End point timeframe:

From Dose 4 to 1 Month After Dose 4 (up to 1 month)

Notes:

[14] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analysed for this endpoint

End point values	Group 1: c7vPnC and Prevenar 13 Co-administration	Group 2: c7vPnC and Prevenar 13 Staggered Administration	Group 3: Prevenar 13 as Control With Supplemental c7vPnC Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	110	85	101	
Units: Percentage of Subjects				
number (confidence interval 95%)	23.6 (16.1 to 32.7)	15.3 (8.4 to 24.7)	25.7 (17.6 to 35.4)	

Statistical analyses

No statistical analyses for this end point

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

End point title	Percentage of Subjects With Adverse Events (AEs) From Supplemental Dose to 1 Month After Supplemental Dose[15][16]

End point description:

An AE was any untoward medical occurrence in study subjects who received study vaccine without regard to possibility of causal relationship with the treatment. Supplemental dose safety analysis set included subjects who received Supplemental Dose and had safety data between Supplemental Dose and 1 month after Supplemental Dose. Data for this endpoint was planned to be collected and analyzed only for Prevenar 13 as control with supplemental c7vPnC dose arm and not planned to be collected and analyzed for c7vPnC and Prevenar 13 co-administration and c7vPnC and Prevenar 13 staggered administration, as pre-specified in protocol.

End point type	Primary

End point timeframe:

From Supplemental Dose to 1 Month After Supplemental Dose (up to 1 month)

Notes:

[15] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analysed for this endpoint

[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 analyzed only for the reporting arm specified

End point values	Group 3: Prevenar 13 as Control With Supplemental c7vPnC Dose			
Subject group type	Reporting group			
Number of subjects analysed	88			
Units: Percentage of Subjects				
number (confidence interval 95%)	18.2 (10.8 to 27.8)			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Serious Adverse Events (SAEs) From Dose 1 to End of the Study

End point title	Percentage of Subjects With Serious Adverse Events (SAEs) From Dose 1 to End of the Study[17]

End point description:

An SAE was any untoward medical occurrence at any dose that results in death; is life-threatening (immediate risk of death); requires inpatient hospitalisation or prolongation of existing hospitalisation; results in persistent or significant disability/incapacity (substantial disruption of the ability to conduct normal life functions); results in congenital anomaly/birth defect or that is considered to be an important medical event. The overall safety population included all subjects who received at least 1 dose of c7vPnC (in Groups 1 and 2) or Prevenar 13 (in Group 3) and had safety data reported in the study.

End point type	Primary

End point timeframe:

From Dose 1 to End of the Study (up to 17 months)

Notes:

[17] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analysed for this endpoint

End point values	Group 1: c7vPnC and Prevenar 13 Co-administration	Group 2: c7vPnC and Prevenar 13 Staggered Administration	Group 3: Prevenar 13 as Control With Supplemental c7vPnC Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	171	147	166	
Units: Percentage of Subjects				
number (confidence interval 95%)	4.1 (1.7 to 8.3)	2.7 (0.7 to 6.8)	5.4 (2.5 to 10.0)	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Newly Diagnosed Chronic Medical Conditions (NDCMCs) From Dose 1 to End of the Study

End point title	Percentage of Subjects With Newly Diagnosed Chronic Medical Conditions (NDCMCs) From Dose 1 to End of the Study[18]

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. The overall safety population included all subjects who received at least 1 dose of c7vPnC (in Groups 1 and 2) or Prevenar 13 (in Group 3) and had safety data reported in the study.

End point type	Primary

End point timeframe:

From Dose 1 to End of the Study (up to 17 months)

Notes:

[18] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analysed for this endpoint

End point values	Group 1: c7vPnC and Prevenar 13 Co-administration	Group 2: c7vPnC and Prevenar 13 Staggered Administration	Group 3: Prevenar 13 as Control With Supplemental c7vPnC Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	171	147	166	
Units: Percentage of Subjects				
number (confidence interval 95%)	7.6 (4.1 to 12.6)	3.4 (1.1 to 7.8)	7.2 (3.8 to 12.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Pneumococcal Serotype-specific Immunoglobulin G (IgG) Geometric Mean Concentration (GMC) 1 Month After Dose 3

End point title	Pneumococcal Serotype-specific Immunoglobulin G (IgG) Geometric Mean Concentration (GMC) 1 Month After Dose 3

End point description:

IgG GMCs were determined for each of 7 pneumococcal serotypes (8, 10A, 11A, 12F, 15B, 22F, and 33F). Dose 3 evaluable immunogenicity population: included all eligible subjects, who were randomly assigned to receive the vaccine, aged 42-98 days on the day of Dose 1 for Groups 1 and 3 or aged 63 to 133 days on the day of Dose 1 for Group 2, received 3 doses of assigned vaccine, had valid determinate IgG concentration for at least 1 serotype from 1 month after Dose 3 visit, had blood collection within 27-56 days, inclusive, after Dose 3, and had no major protocol deviations.

End point type	Secondary

End point timeframe:

1 Month After Dose 3

End point values	Group 1: c7vPnC and Prevenar 13 Co-administration	Group 2: c7vPnC and Prevenar 13 Staggered Administration	Group 3: Prevenar 13 as Control With Supplemental c7vPnC Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	128	107	109	
Units: microgram per milliliter				
geometric mean (confidence interval 95%)				
Serotype 8	2.90 (2.47 to 3.39)	5.14 (4.41 to 5.99)	0.03 (0.03 to 0.04)	
Serotype 10A	2.55 (1.95 to 3.34)	4.52 (3.59 to 5.69)	0.03 (0.03 to 0.04)	

Serotype 11A	4.37 (3.57 to 5.34)	8.88 (7.25 to 10.87)	0.01 (0.01 to 0.02)	
Serotype 12F	1.92 (1.58 to 2.34)	3.35 (2.75 to 4.07)	0.02 (0.02 to 0.02)	
Serotype 15B	9.12 (7.54 to 11.04)	14.86 (12.65 to 17.44)	0.05 (0.04 to 0.06)	
Serotype 22F	9.25 (7.50 to 11.41)	23.94 (19.88 to 28.82)	0.01 (0.01 to 0.01)	
Serotype 33F	3.40 (2.75 to 4.21)	4.83 (3.99 to 5.84)	0.06 (0.05 to 0.06)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Achieving Prespecified Level of Pnuemococcal Serotype-specific Immunoglobulin G (IgG) Concentrations 1 Month After Dose 3

End point title	Percentage of Subjects Achieving Prespecified Level of Pnuemococcal Serotype-specific Immunoglobulin G (IgG) Concentrations 1 Month After Dose 3

End point description:

Percentage of subjects with pre-specified IgG concentration >=0.35 microgram per milliliter were determined for each of 7 pneumococcal serotypes (8, 10A, 11A, 12F, 15B, 22F, and 33F). Dose 3 evaluable immunogenicity population: included all eligible subjects, who were randomly assigned to receive the vaccine, aged 42-98 days on the day of Dose 1 for Groups 1 and 3 or aged 63 to 133 days on the day of Dose 1 for Group 2, received 3 doses of assigned vaccine, had valid determinate IgG concentration for at least 1 serotype from 1 month after Dose 3 visit, had blood collection within 27-56 days, inclusive, after Dose 3, and had no major protocol deviations.

End point type	Secondary

End point timeframe:

1 Month after Dose 3

End point values	Group 1: c7vPnC and Prevenar 13 Co-administration	Group 2: c7vPnC and Prevenar 13 Staggered Administration	Group 3: Prevenar 13 as Control With Supplemental c7vPnC Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	128	107	109	
Units: Percentage of Subjects				
number (confidence interval 95%)				
Serotype 8	98.4 (94.5 to 99.8)	100.0 (96.6 to 100.0)	1.8 (0.2 to 6.5)	
Serotype 10A	89.8 (83.3 to 94.5)	98.1 (93.4 to 99.8)	2.8 (0.6 to 7.8)	
Serotype 11A	96.9 (92.2 to 99.1)	99.1 (94.9 to 100.0)	0.9 (0.0 to 5.0)	
Serotype 12F	95.3 (90.1 to 98.3)	98.1 (93.4 to 99.8)	0.0 (0.0 to 3.3)	
Serotype 15B	96.9 (92.2 to 99.1)	100.0 (96.6 to 100.0)	6.4 (2.6 to 12.8)	
Serotype 22F	96.9 (92.2 to 99.1)	100.0 (96.6 to 100.0)	0.0 (0.0 to 3.3)	

Serotype 33F	96.1 (91.1 to 98.7)	99.1 (94.9 to 100.0)	4.6 (1.5 to 10.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Pneumococcal Serotype-specific Immunoglobulin G (IgG) Geometric Mean Concentration (GMC) 1 Month After Dose 4

End point title	Pneumococcal Serotype-specific Immunoglobulin G (IgG) Geometric Mean Concentration (GMC) 1 Month After Dose 4

End point description:

IgG GMCs were determined for each of 7 pneumococcal serotypes (8, 10A, 11A, 12F, 15B, 22F, and 33F). Dose 4 evaluable immunogenicity population: eligible subjects, randomly assigned to receive vaccine, aged 42-98 days on the day of Dose 1 for Groups 1 and 3 or aged 63 to 133 days on the day of Dose 1 for Group 2, received all 4 doses of assigned vaccine, with Dose 4 received in defined window (365-386 days of age), had valid determinate IgG concentration for at least 1 serotype 1 month post dose 4,had blood collection within 27-56 days post Dose 4, and had no major protocol deviations.

End point type	Secondary

End point timeframe:

1 Month After Dose 4

End point values	Group 1: c7vPnC and Prevenar 13 Co-administration	Group 2: c7vPnC and Prevenar 13 Staggered Administration	Group 3: Prevenar 13 as Control With Supplemental c7vPnC Dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	76	57	68	
Units: microgram per milliliter				
geometric mean (confidence interval 95%)				
Serotype 8	3.79 (3.10 to 4.62)	3.05 (2.46 to 3.78)	0.08 (0.06 to 0.12)	
Serotype 10A	12.77 (10.16 to 16.06)	7.15 (5.26 to 9.72)	0.04 (0.03 to 0.04)	
Serotype 11A	8.25 (6.72 to 10.12)	7.12 (5.53 to 9.15)	0.02 (0.01 to 0.04)	
Serotype 12F	3.15 (2.64 to 3.74)	2.57 (2.08 to 3.19)	0.03 (0.02 to 0.03)	
Serotype 15B	24.56 (21.23 to 28.41)	17.70 (14.31 to 21.89)	0.06 (0.04 to 0.07)	
Serotype 22F	25.68 (21.33 to 30.91)	29.92 (24.21 to 36.98)	0.01 (0.01 to 0.02)	
Serotype 33F	5.38 (4.47 to 6.48)	3.95 (3.16 to 4.93)	0.06 (0.05 to 0.08)	

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 Dose 1,2,3,4,Supplemental Dose(SD);Non-SAEs:from Dose 1 to 1 month after Dose 3,Dose 4 to 1 month after Dose 4,SD to 1 month after SD;SAEs:Dose 1 to 6 months after last dose (Dose 4 or SD)

Adverse event reporting additional description:

Same event may appear as AE and SAE, what is presented are distinct events. Event may be categorized as serious in 1 subject and as non-serious in another subject or 1 subject may have experienced both serious and non-serious event during study. Overall safety analysis set was analysed.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups

Reporting group title	Group 1: c7vPnC and Prevenar 13 Co-administration

Reporting group description:

Subjects who received a dose of c7vPnC in one leg and Prevenar 13 and other vaccines in the other leg at 2, 4, 6, and 12 months of age (Dose 1, 2, 3, and 4 respectively).

Reporting group title	Group 2: c7vPnC and Prevenar 13 Staggered Administration

Reporting group description:

Subjects who received a dose of c7vPnC at 3, 5, 7, and 13 months of age in one leg (Dose 1, 2, 3, and 4 respectively) and Prevenar 13 in the other leg at 2, 4, 6, and 12 month of age.

Reporting group title	Group 3: Prevenar 13 as Control With Supplemental c7vPnC Dose

Reporting group description:

Subjects who received a dose of Prevenar 13 at 2, 4, 6, and 12 months of age (Dose 1, 2, 3, and 4 respectively) and a dose of c7vPnC at 13 months (Supplemental Dose).

Serious adverse events	Group 1: c7vPnC and Prevenar 13 Co-administration	Group 2: c7vPnC and Prevenar 13 Staggered Administration	Group 3: Prevenar 13 as Control With Supplemental c7vPnC Dose
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 171 (4.09%)	4 / 147 (2.72%)	9 / 166 (5.42%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Post procedural haemorrhage			
subjects affected / exposed	0 / 171 (0.00%)	0 / 147 (0.00%)	1 / 166 (0.60%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome			
subjects affected / exposed	0 / 171 (0.00%)	0 / 147 (0.00%)	1 / 166 (0.60%)

occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute respiratory failure			
subjects affected / exposed	0 / 171 (0.00%)	0 / 147 (0.00%)	1 / 166 (0.60%)
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 / 171 (0.58%)	0 / 147 (0.00%)	0 / 166 (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
Status epilepticus			
subjects affected / exposed	1 / 171 (0.58%)	0 / 147 (0.00%)	0 / 166 (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
Metabolism and nutrition disorders			
Failure to thrive			
subjects affected / exposed	1 / 171 (0.58%)	0 / 147 (0.00%)	0 / 166 (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			
Bronchiolitis			
subjects affected / exposed	2 / 171 (1.17%)	1 / 147 (0.68%)	3 / 166 (1.81%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 171 (0.00%)	1 / 147 (0.68%)	0 / 166 (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
Parotid abscess			
subjects affected / exposed	0 / 171 (0.00%)	1 / 147 (0.68%)	0 / 166 (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
Periorbital cellulitis			

subjects affected / exposed	1 / 171 (0.58%)	0 / 147 (0.00%)	0 / 166 (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
Pneumonia viral			
subjects affected / exposed	0 / 171 (0.00%)	0 / 147 (0.00%)	2 / 166 (1.20%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus bronchiolitis			
subjects affected / exposed	0 / 171 (0.00%)	0 / 147 (0.00%)	1 / 166 (0.60%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus infection			
subjects affected / exposed	0 / 171 (0.00%)	0 / 147 (0.00%)	1 / 166 (0.60%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subcutaneous abscess			
subjects affected / exposed	0 / 171 (0.00%)	1 / 147 (0.68%)	0 / 166 (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
Urinary tract infection			
subjects affected / exposed	1 / 171 (0.58%)	1 / 147 (0.68%)	0 / 166 (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
Viral infection			
subjects affected / exposed	0 / 171 (0.00%)	0 / 147 (0.00%)	1 / 166 (0.60%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Group 1: c7vPnC and Prevenar 13 Co-administration	Group 2: c7vPnC and Prevenar 13 Staggered Administration	Group 3: Prevenar 13 as Control With Supplemental c7vPnC Dose
Total subjects affected by non-serious adverse events			
subjects affected / exposed	163 / 171 (95.32%)	138 / 147 (93.88%)	163 / 166 (98.19%)
Immune system disorders			
Food allergy			
subjects affected / exposed	2 / 171 (1.17%)	0 / 147 (0.00%)	0 / 166 (0.00%)
occurrences (all)	2	0	0
Hypersensitivity			
subjects affected / exposed	3 / 171 (1.75%)	0 / 147 (0.00%)	0 / 166 (0.00%)
occurrences (all)	3	0	0
Milk allergy			
subjects affected / exposed	2 / 171 (1.17%)	0 / 147 (0.00%)	0 / 166 (0.00%)
occurrences (all)	2	0	0
Seasonal allergy			
subjects affected / exposed	2 / 171 (1.17%)	0 / 147 (0.00%)	2 / 166 (1.20%)
occurrences (all)	2	0	2
General disorders and administration site conditions			
Injection site erythema (REDNESS)			
alternative assessment type: Systematic			
subjects affected / exposed	82 / 171 (47.95%)	67 / 147 (45.58%)	77 / 166 (46.39%)
occurrences (all)	157	109	135
Injection site pain (PAIN)			
alternative assessment type: Systematic			
subjects affected / exposed	131 / 171 (76.61%)	82 / 147 (55.78%)	112 / 166 (67.47%)
occurrences (all)	287	143	251
Injection site swelling (SWELLING)			
alternative assessment type: Systematic			
subjects affected / exposed	74 / 171 (43.27%)	49 / 147 (33.33%)	68 / 166 (40.96%)
occurrences (all)	143	93	136
Pyrexia			
subjects affected / exposed	5 / 171 (2.92%)	8 / 147 (5.44%)	7 / 166 (4.22%)
occurrences (all)	5	8	8
Pyrexia (FEVER)			
alternative assessment type: Systematic			
subjects affected / exposed	62 / 171 (36.26%)	20 / 147 (13.61%)	53 / 166 (31.93%)

occurrences (all)	94	22	79

Psychiatric disorders			
Irritability (IRRITABILITY)			
alternative assessment type: Systematic			
subjects affected / exposed	141 / 171 (82.46%)	113 / 147 (76.87%)	141 / 166 (84.94%)
occurrences (all)	440	303	413
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	1 / 171 (0.58%)	2 / 147 (1.36%)	2 / 166 (1.20%)
occurrences (all)	1	3	2
Contusion			
subjects affected / exposed	2 / 171 (1.17%)	0 / 147 (0.00%)	0 / 166 (0.00%)
occurrences (all)	2	0	0
Fall			
subjects affected / exposed	2 / 171 (1.17%)	1 / 147 (0.68%)	0 / 166 (0.00%)
occurrences (all)	2	1	0
Head injury			
subjects affected / exposed	2 / 171 (1.17%)	3 / 147 (2.04%)	0 / 166 (0.00%)
occurrences (all)	2	3	0
Congenital, familial and genetic disorders			
Craniosynostosis			
subjects affected / exposed	0 / 171 (0.00%)	2 / 147 (1.36%)	0 / 166 (0.00%)
occurrences (all)	0	2	0
Plagiocephaly			
subjects affected / exposed	0 / 171 (0.00%)	0 / 147 (0.00%)	4 / 166 (2.41%)
occurrences (all)	0	0	4
Blood and lymphatic system disorders			
Iron deficiency anaemia			
subjects affected / exposed	1 / 171 (0.58%)	2 / 147 (1.36%)	2 / 166 (1.20%)
occurrences (all)	1	2	2
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	4 / 171 (2.34%)	7 / 147 (4.76%)	4 / 166 (2.41%)
occurrences (all)	4	7	4
Bronchial hyperreactivity			

subjects affected / exposed	1 / 171 (0.58%)	0 / 147 (0.00%)	2 / 166 (1.20%)
occurrences (all)	1	0	4
Cough			
subjects affected / exposed	9 / 171 (5.26%)	4 / 147 (2.72%)	10 / 166 (6.02%)
occurrences (all)	9	4	12
Nasal congestion			
subjects affected / exposed	10 / 171 (5.85%)	5 / 147 (3.40%)	5 / 166 (3.01%)
occurrences (all)	10	5	6
Rhinitis allergic			
subjects affected / exposed	3 / 171 (1.75%)	5 / 147 (3.40%)	3 / 166 (1.81%)
occurrences (all)	3	5	3
Wheezing			
subjects affected / exposed	3 / 171 (1.75%)	3 / 147 (2.04%)	3 / 166 (1.81%)
occurrences (all)	3	4	3
Nervous system disorders			
Somnolence (DROWSINESS)			
alternative assessment type: Systematic			
subjects affected / exposed	124 / 171 (72.51%)	80 / 147 (54.42%)	126 / 166 (75.90%)
occurrences (all)	312	156	294
Ear and labyrinth disorders			
Cerumen impaction			
subjects affected / exposed	2 / 171 (1.17%)	0 / 147 (0.00%)	1 / 166 (0.60%)
occurrences (all)	2	0	1
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	8 / 171 (4.68%)	8 / 147 (5.44%)	3 / 166 (1.81%)
occurrences (all)	9	9	4
Diarrhoea			
subjects affected / exposed	5 / 171 (2.92%)	6 / 147 (4.08%)	8 / 166 (4.82%)
occurrences (all)	6	7	9
Gastritis			
subjects affected / exposed	0 / 171 (0.00%)	0 / 147 (0.00%)	2 / 166 (1.20%)
occurrences (all)	0	0	2
Gastrooesophageal reflux disease			
subjects affected / exposed	6 / 171 (3.51%)	2 / 147 (1.36%)	4 / 166 (2.41%)
occurrences (all)	6	2	5

Teething			
subjects affected / exposed	4 / 171 (2.34%)	0 / 147 (0.00%)	5 / 166 (3.01%)
occurrences (all)	4	0	5
Vomiting			
subjects affected / exposed	5 / 171 (2.92%)	1 / 147 (0.68%)	5 / 166 (3.01%)
occurrences (all)	5	1	6
Skin and subcutaneous tissue disorders			
Dermatitis atopic			
subjects affected / exposed	11 / 171 (6.43%)	5 / 147 (3.40%)	12 / 166 (7.23%)
occurrences (all)	11	5	12
Dermatitis diaper			
subjects affected / exposed	11 / 171 (6.43%)	7 / 147 (4.76%)	5 / 166 (3.01%)
occurrences (all)	11	7	7
Eczema			
subjects affected / exposed	5 / 171 (2.92%)	2 / 147 (1.36%)	2 / 166 (1.20%)
occurrences (all)	5	3	2
Rash			
subjects affected / exposed	4 / 171 (2.34%)	1 / 147 (0.68%)	2 / 166 (1.20%)
occurrences (all)	4	2	2
Seborrhoea			
subjects affected / exposed	0 / 171 (0.00%)	0 / 147 (0.00%)	3 / 166 (1.81%)
occurrences (all)	0	0	3
Seborrhoeic dermatitis			
subjects affected / exposed	2 / 171 (1.17%)	0 / 147 (0.00%)	4 / 166 (2.41%)
occurrences (all)	2	0	4
Musculoskeletal and connective tissue disorders			
Torticollis			
subjects affected / exposed	0 / 171 (0.00%)	0 / 147 (0.00%)	2 / 166 (1.20%)
occurrences (all)	0	0	2
Metabolism and nutrition disorders			
Decreased appetite (DECREASED APPETITE)			
alternative assessment type: Systematic			
subjects affected / exposed	82 / 171 (47.95%)	51 / 147 (34.69%)	84 / 166 (50.60%)
occurrences (all)	149	82	157
Infections and infestations			

Acute sinusitis			
subjects affected / exposed	2 / 171 (1.17%)	0 / 147 (0.00%)	2 / 166 (1.20%)
occurrences (all)	2	0	2
Body tinea			
subjects affected / exposed	2 / 171 (1.17%)	1 / 147 (0.68%)	2 / 166 (1.20%)
occurrences (all)	2	1	2
Bronchiolitis			
subjects affected / exposed	13 / 171 (7.60%)	6 / 147 (4.08%)	14 / 166 (8.43%)
occurrences (all)	15	7	14
Bronchitis			
subjects affected / exposed	5 / 171 (2.92%)	7 / 147 (4.76%)	3 / 166 (1.81%)
occurrences (all)	5	7	3
Conjunctivitis			
subjects affected / exposed	13 / 171 (7.60%)	8 / 147 (5.44%)	11 / 166 (6.63%)
occurrences (all)	14	10	12
Candida infection			
subjects affected / exposed	0 / 171 (0.00%)	2 / 147 (1.36%)	3 / 166 (1.81%)
occurrences (all)	0	2	3
Conjunctivitis bacterial			
subjects affected / exposed	2 / 171 (1.17%)	1 / 147 (0.68%)	4 / 166 (2.41%)
occurrences (all)	2	1	4
Croup infectious			
subjects affected / exposed	3 / 171 (1.75%)	2 / 147 (1.36%)	5 / 166 (3.01%)
occurrences (all)	4	2	5
Exanthema subitum			
subjects affected / exposed	2 / 171 (1.17%)	2 / 147 (1.36%)	0 / 166 (0.00%)
occurrences (all)	2	2	0
Gastroenteritis			
subjects affected / exposed	2 / 171 (1.17%)	2 / 147 (1.36%)	3 / 166 (1.81%)
occurrences (all)	2	2	3
Gastroenteritis viral			
subjects affected / exposed	0 / 171 (0.00%)	1 / 147 (0.68%)	2 / 166 (1.20%)
occurrences (all)	0	1	3
Hand-foot-and-mouth disease			
subjects affected / exposed	3 / 171 (1.75%)	0 / 147 (0.00%)	2 / 166 (1.20%)
occurrences (all)	3	0	2

Impetigo			
subjects affected / exposed	0 / 171 (0.00%)	2 / 147 (1.36%)	1 / 166 (0.60%)
occurrences (all)	0	2	1
Influenza			
subjects affected / exposed	3 / 171 (1.75%)	7 / 147 (4.76%)	5 / 166 (3.01%)
occurrences (all)	3	7	5
Laryngitis			
subjects affected / exposed	0 / 171 (0.00%)	4 / 147 (2.72%)	0 / 166 (0.00%)
occurrences (all)	0	4	0
Nasopharyngitis			
subjects affected / exposed	4 / 171 (2.34%)	1 / 147 (0.68%)	3 / 166 (1.81%)
occurrences (all)	4	1	3
Otitis media			
subjects affected / exposed	11 / 171 (6.43%)	17 / 147 (11.56%)	13 / 166 (7.83%)
occurrences (all)	13	22	15
Oral candidiasis			
subjects affected / exposed	2 / 171 (1.17%)	3 / 147 (2.04%)	2 / 166 (1.20%)
occurrences (all)	2	3	2
Otitis media acute			
subjects affected / exposed	6 / 171 (3.51%)	2 / 147 (1.36%)	6 / 166 (3.61%)
occurrences (all)	8	3	14
Pharyngitis			
subjects affected / exposed	4 / 171 (2.34%)	6 / 147 (4.08%)	4 / 166 (2.41%)
occurrences (all)	5	7	5
Pneumonia			
subjects affected / exposed	1 / 171 (0.58%)	1 / 147 (0.68%)	2 / 166 (1.20%)
occurrences (all)	1	1	2
Respiratory syncytial virus bronchiolitis			
subjects affected / exposed	0 / 171 (0.00%)	1 / 147 (0.68%)	3 / 166 (1.81%)
occurrences (all)	0	1	3
Respiratory syncytial virus infection			
subjects affected / exposed	1 / 171 (0.58%)	2 / 147 (1.36%)	1 / 166 (0.60%)
occurrences (all)	1	2	1
Respiratory tract infection viral			
subjects affected / exposed	1 / 171 (0.58%)	2 / 147 (1.36%)	1 / 166 (0.60%)
occurrences (all)	1	2	1

Roseola			
subjects affected / exposed	0 / 171 (0.00%)	0 / 147 (0.00%)	2 / 166 (1.20%)
occurrences (all)	0	0	2
Sinusitis			
subjects affected / exposed	1 / 171 (0.58%)	3 / 147 (2.04%)	0 / 166 (0.00%)
occurrences (all)	1	3	0
Tonsillitis			
subjects affected / exposed	3 / 171 (1.75%)	0 / 147 (0.00%)	0 / 166 (0.00%)
occurrences (all)	3	0	0
Upper respiratory tract infection			
subjects affected / exposed	45 / 171 (26.32%)	43 / 147 (29.25%)	35 / 166 (21.08%)
occurrences (all)	65	58	47
Urinary tract infection			
subjects affected / exposed	3 / 171 (1.75%)	1 / 147 (0.68%)	0 / 166 (0.00%)
occurrences (all)	3	2	0
Viral infection			
subjects affected / exposed	5 / 171 (2.92%)	4 / 147 (2.72%)	7 / 166 (4.22%)
occurrences (all)	7	4	7
Viral upper respiratory tract infection			
subjects affected / exposed	4 / 171 (2.34%)	4 / 147 (2.72%)	4 / 166 (2.41%)
occurrences (all)	4	6	5

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 February 2020	Updated the number of subjects per arm and the probabilities of detecting AEs by frequency, and minor modifications were made to the target numbers for the OPA and diphtheria/pertussis subsets.

Notes:

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.

Total 565 subjects were randomized. 512 subjects from 39 sites, and 53 subjects from 2 sites terminated early due to serious quality issues. Data from 2 terminated sites/53 were not included in safety or evaluable immunogenicity populations/analyses.

Notes: