Clinical trial results:
A Phase 3, Randomized, Double-blind Trial to Evaluate the Safety and Immunogenicity of a 20-valent Pneumococcal Conjugate Vaccine in Pneumococcal Vaccine–naïve Adults 18 Years of age and Older

Summary

EudraCT number	2018-004279-11
Trial protocol	SE
Global end of trial date	16 December 2019

Results information

Result version number	v1 (current)
This version publication date	17 December 2020
First version publication date	17 December 2020

Trial information

Trial identification

Sponsor protocol code	B7471007

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03760146
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 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., +1 8007181021, 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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	09 April 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	16 December 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

• Safety: To describe the safety profile of 20-valent pneumococcal conjugate vaccine (20vPnC) in adults 18 years of age and older. • Immunogenicity: To demonstrate that the immune responses to the 13 serotypes in 13-valent pneumococcal conjugate vaccine (13vPnC) (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F) induced by 20vPnC in adults 60 years of age and older are noninferior to the immune response induced by 13vPnC. • To demonstrate that the immune responses to the 7 additional serotypes (8, 10A, 11A, 12F, 15B, 22F, and 33F) induced by 20vPnC in adults 60 years of age and older are noninferior to the immune response induced by 23-valent pneumococcal polysaccharide vaccine (PPSV23).

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 December 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	Sweden: 172
Country: Number of subjects enrolled	United States: 3730
Worldwide total number of subjects	3902
EEA total number of subjects	172

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	2881
From 65 to 84 years	1010
85 years and over	11

Subject disposition

Recruitment

Recruitment details:

This study was conducted from 12 December 2018 to 16 December 2019 in the United States and Sweden.

Pre-assignment

Screening details:

A total of 3902 subjects aged greater than or equal to (>=) 18 years at baseline, were enrolled into the study. Out of these 3902 subjects, 3889 subjects received study vaccination.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1: 20vPnC/Saline

Arm description:

Subjects aged 60 years and above were randomized to receive a single dose of 0.5 milliliter (mL) intramuscular injection of 20-valent pneumococcal vaccine (20vPnC) at Vaccination 1 (Day 1) and a single dose of 0.5 mL intramuscular injection of saline at Vaccination 2 (28 to 42 days after Vaccination 1).

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

Dosage and administration details:

Subjects received a single 0.5 mL intramuscular injection of saline at Vaccination 2 (28 to 42 days after Vaccination 1).

Investigational medicinal product name	20vPnC
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received a single 0.5 mL intramuscular injection of 20vPnC at Vaccination 1 (Day 1).

Arm title	Cohort 1: 13vPnC/PPSV23

Arm description:

Subjects aged 60 years and above were randomized to receive a single dose of 0.5 mL intramuscular injection of 13-valent pneumococcal vaccine (13vPnC) at Vaccination 1 (Day 1) and a single dose of 0.5 mL intramuscular injection of 23-valent pneumococcal polysaccharide vaccine (PPSV23) at Vaccination 2 (28 to 42 days after vaccination 1).

Arm type	Active comparator

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 a single 0.5 mL intramuscular injection of 13vPnC at Vaccination 1 (Day 1)

Investigational medicinal product name	PPSV23
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 0.5 mL intramuscular injection of PPSV23 at Vaccination 2 (28 to 42 days after Vaccination2).

Arm title	Cohort 2: 20vPnC

Arm description:

Subjects aged 50 through 59 years were randomized to receive a single dose of 0.5 mL intramuscular injection of 20vPnC (Day 1).

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

Dosage and administration details:

Subjects received a single 0.5 mL intramuscular injection of 20vPnC (Day 1).

Arm title	Cohort 2: 13vPnC

Arm description:

Subjects aged 50 through 59 years were randomized to receive a single dose of 0.5 mL intramuscular injection of 13vPnC (Day 1).

Arm type	Active comparator
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 a single 0.5 mL intramuscular injection of 13vPnC (Day 1).

Arm title	Cohort 3: 20vPnC

Arm description:

Subjects aged 18 through 49 years were randomized to receive a single dose of 0.5 mL intramuscular injection of 20vPnC (Day 1).

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

Dosage and administration details:

Subjects received a single 0.5 mL intramuscular injection of 20vPnC (Day 1).

Arm title	Cohort 3: 13vPnC

Arm description:

Subjects aged 18 through 49 years were randomized to receive a single dose of 0.5 mL intramuscular injection of 13vPnC (Day 1).

Arm type	Active comparator
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 a single 0.5 mL intramuscular injection of 13vPnC (Day 1).

Number of subjects in period 1	Cohort 1: 20vPnC/Saline	Cohort 1: 13vPnC/PPSV23	Cohort 2: 20vPnC
Started	1514	1495	334
Vaccination 1	1507	1490	334
Vaccination 2	1461	1446	0 [1]
Evaluable-20 Immunogenicity	946 [2]	0 [3]	321 [4]
Evaluable 13-Matched Immunogenicity	1435	1420	0 [5]
Evaluable 7-Additional Immunogenicity	1433	1383 [6]	0 [7]
Safety Population	1507	1490	334
Completed	1418	1417	323
Not completed	96	78	11
Adverse event, serious fatal	1	-	-
Consent withdrawn by subject	19	20	1
Adverse event, non-fatal	11	8	-
No longer met eligibility criteria	3	9	-
Lost to follow-up	41	28	9
Protocol deviation	21	13	1

Number of subjects in period 1	Cohort 2: 13vPnC	Cohort 3: 20vPnC	Cohort 3: 13vPnC
Started	111	336	112
Vaccination 1	111	335	112
Vaccination 2	0 [8]	0 [9]	0 [10]
Evaluable-20 Immunogenicity	0 [11]	317 [12]	0 [13]
Evaluable 13-Matched Immunogenicity	0 [14]	0 [15]	0 [16]
Evaluable 7-Additional Immunogenicity	0 [17]	0 [18]	0 [19]
Safety Population	111	335	112
Completed	109	319	104
Not completed	2	17	8
Adverse event, serious fatal	-	-	-
Consent withdrawn by subject	-	1	-

Adverse event, non-fatal	-	-	-
No longer met eligibility criteria	-	1	-
Lost to follow-up	2	14	8
Protocol deviation	-	1	-

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Evaluable-20 immunogenicity population included subjects who were enrolled in the appropriate cohort based on age, received Vaccination 1 as randomized, had at least 1 valid OPA titer from the blood collection 27 to 49 days after 20vPnC, had no other major protocol deviations.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Evaluable-20 immunogenicity population included subjects who were enrolled in the appropriate cohort based on age, received Vaccination 1 as randomized, had at least 1 valid OPA titer from the blood collection 27 to 49 days after 20vPnC, had no other major protocol deviations.

[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Evaluable-20 immunogenicity population included subjects who were enrolled in the appropriate cohort based on age, received Vaccination 1 as randomized, had at least 1 valid OPA titer from the blood collection 27 to 49 days after 20vPnC, had no other major protocol deviations.

[4] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Evaluable-20 immunogenicity population included subjects who were enrolled in the appropriate cohort based on age, received Vaccination 1 as randomized, had at least 1 valid OPA titer from the blood collection 27 to 49 days after 20vPnC, had no other major protocol deviations.

[5] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Evaluable-20 immunogenicity population included subjects who were enrolled in the appropriate cohort based on age, received Vaccination 1 as randomized, had at least 1 valid OPA titer from the blood collection 27 to 49 days after 20vPnC, had no other major protocol deviations.

[6] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Evaluable-20 immunogenicity population included subjects who were enrolled in the appropriate cohort based on age, received Vaccination 1 as randomized, had at least 1 valid OPA titer from the blood collection 27 to 49 days after 20vPnC, had no other major protocol deviations.

[7] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Evaluable-20 immunogenicity population included subjects who were enrolled in the appropriate cohort based on age, received Vaccination 1 as randomized, had at least 1 valid OPA titer from the blood collection 27 to 49 days after 20vPnC, had no other major protocol deviations.

[8] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Evaluable-20 immunogenicity population included subjects who were enrolled in the appropriate cohort based on age, received Vaccination 1 as randomized, had at least 1 valid OPA titer from the blood collection 27 to 49 days after 20vPnC, had no other major protocol deviations.

[9] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Evaluable-20 immunogenicity population included subjects who were enrolled in the appropriate cohort based on age, received Vaccination 1 as randomized, had at least 1 valid OPA titer from the blood collection 27 to 49 days after 20vPnC, had no other major protocol deviations.

[10] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Evaluable-20 immunogenicity population included subjects who were enrolled in the

appropriate cohort based on age, received Vaccination 1 as randomized, had at least 1 valid OPA titer from the blood collection 27 to 49 days after 20vPnC, had no other major protocol deviations.
[11] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Evaluable-20 immunogenicity population included subjects who were enrolled in the appropriate cohort based on age, received Vaccination 1 as randomized, had at least 1 valid OPA titer from the blood collection 27 to 49 days after 20vPnC, had no other major protocol deviations.
[12] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Evaluable-20 immunogenicity population included subjects who were enrolled in the appropriate cohort based on age, received Vaccination 1 as randomized, had at least 1 valid OPA titer from the blood collection 27 to 49 days after 20vPnC, had no other major protocol deviations.
[13] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Evaluable-20 immunogenicity population included subjects who were enrolled in the appropriate cohort based on age, received Vaccination 1 as randomized, had at least 1 valid OPA titer from the blood collection 27 to 49 days after 20vPnC, had no other major protocol deviations.
[14] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Evaluable-20 immunogenicity population included subjects who were enrolled in the appropriate cohort based on age, received Vaccination 1 as randomized, had at least 1 valid OPA titer from the blood collection 27 to 49 days after 20vPnC, had no other major protocol deviations.
[15] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Evaluable-20 immunogenicity population included subjects who were enrolled in the appropriate cohort based on age, received Vaccination 1 as randomized, had at least 1 valid OPA titer from the blood collection 27 to 49 days after 20vPnC, had no other major protocol deviations.
[16] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Evaluable-20 immunogenicity population included subjects who were enrolled in the appropriate cohort based on age, received Vaccination 1 as randomized, had at least 1 valid OPA titer from the blood collection 27 to 49 days after 20vPnC, had no other major protocol deviations.
[17] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Evaluable-20 immunogenicity population included subjects who were enrolled in the appropriate cohort based on age, received Vaccination 1 as randomized, had at least 1 valid OPA titer from the blood collection 27 to 49 days after 20vPnC, had no other major protocol deviations.
[18] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Evaluable-20 immunogenicity population included subjects who were enrolled in the appropriate cohort based on age, received Vaccination 1 as randomized, had at least 1 valid OPA titer from the blood collection 27 to 49 days after 20vPnC, had no other major protocol deviations.
[19] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Evaluable-20 immunogenicity population included subjects who were enrolled in the appropriate cohort based on age, received Vaccination 1 as randomized, had at least 1 valid OPA titer from the blood collection 27 to 49 days after 20vPnC, had no other major protocol deviations.

Baseline characteristics

Reporting groups	
Reporting group title	Cohort 1: 20vPnC/Saline
Reporting group description:	
Subjects aged 60 years and above were randomized to receive a single dose of 0.5 milliliter (mL) intramuscular injection of 20-valent pneumococcal vaccine (20vPnC) at Vaccination 1 (Day 1) and a single dose of 0.5 mL intramuscular injection of saline at Vaccination 2 (28 to 42 days after Vaccination 1).	
Reporting group title	Cohort 1: 13vPnC/PPSV23
Reporting group description:	
Subjects aged 60 years and above were randomized to receive a single dose of 0.5 mL intramuscular injection of 13-valent pneumococcal vaccine (13vPnC) at Vaccination 1 (Day 1) and a single dose of 0.5 mL intramuscular injection of 23-valent pneumococcal polysaccharide vaccine (PPSV23) at Vaccination 2 (28 to 42 days after vaccination 1).	
Reporting group title	Cohort 2: 20vPnC
Reporting group description:	
Subjects aged 50 through 59 years were randomized to receive a single dose of 0.5 mL intramuscular injection of 20vPnC (Day 1).	
Reporting group title	Cohort 2: 13vPnC
Reporting group description:	
Subjects aged 50 through 59 years were randomized to receive a single dose of 0.5 mL intramuscular injection of 13vPnC (Day 1).	
Reporting group title	Cohort 3: 20vPnC
Reporting group description:	
Subjects aged 18 through 49 years were randomized to receive a single dose of 0.5 mL intramuscular injection of 20vPnC (Day 1).	
Reporting group title	Cohort 3: 13vPnC
Reporting group description:	
Subjects aged 18 through 49 years were randomized to receive a single dose of 0.5 mL intramuscular injection of 13vPnC (Day 1).	

Reporting group values	Cohort 1: 20vPnC/Saline	Cohort 1: 13vPnC/PPSV23	Cohort 2: 20vPnC
Number of subjects	1514	1495	334
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)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	996	992	334
From 65-84 years	510	500	0
85 years and over	8	3	0
Age Continuous Units: Years			
arithmetic mean	64.6	64.6	54.9
standard deviation	± 4.82	± 4.83	± 2.77

Sex: Female, Male Units: subjects			
Female	900	880	195
Male	614	615	139
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	6	9	0
Asian	19	15	10
Native Hawaiian or Other Pacific Islander	1	1	0
Black or African American	179	212	35
White	1300	1240	278
More than one race	7	9	6
Unknown or Not Reported	2	9	5
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	169	169	12
Not Hispanic or Latino	1329	1312	319
Unknown or Not Reported	16	14	3

Reporting group values	Cohort 2: 13vPnC	Cohort 3: 20vPnC	Cohort 3: 13vPnC
Number of subjects	111	336	112
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)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	111	336	112
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	55.0	34.0	33.9
standard deviation	± 3.11	± 8.76	± 8.03
Sex: Female, Male Units: subjects			
Female	69	214	77
Male	42	122	35
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	3	1	1
Asian	2	11	1
Native Hawaiian or Other Pacific Islander	0	3	1
Black or African American	15	34	7
White	90	275	101
More than one race	1	8	1
Unknown or Not Reported	0	4	0

Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	8	24	7
Not Hispanic or Latino	101	301	102
Unknown or Not Reported	2	11	3

Reporting group values	Total		
Number of subjects	3902		
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)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	2881		
From 65-84 years	1010		
85 years and over	11		
Age Continuous Units: Years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male Units: subjects			
Female	2335		
Male	1567		
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	20		
Asian	58		
Native Hawaiian or Other Pacific Islander	6		
Black or African American	482		
White	3284		
More than one race	32		
Unknown or Not Reported	20		
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	389		
Not Hispanic or Latino	3464		
Unknown or Not Reported	49		

End points

End points reporting groups

Reporting group title	Cohort 1: 20vPnC/Saline
Reporting group description:	
Subjects aged 60 years and above were randomized to receive a single dose of 0.5 milliliter (mL) intramuscular injection of 20-valent pneumococcal vaccine (20vPnC) at Vaccination 1 (Day 1) and a single dose of 0.5 mL intramuscular injection of saline at Vaccination 2 (28 to 42 days after Vaccination 1).	
Reporting group title	Cohort 1: 13vPnC/PPSV23
Reporting group description:	
Subjects aged 60 years and above were randomized to receive a single dose of 0.5 mL intramuscular injection of 13-valent pneumococcal vaccine (13vPnC) at Vaccination 1 (Day 1) and a single dose of 0.5 mL intramuscular injection of 23-valent pneumococcal polysaccharide vaccine (PPSV23) at Vaccination 2 (28 to 42 days after vaccination 1).	
Reporting group title	Cohort 2: 20vPnC
Reporting group description:	
Subjects aged 50 through 59 years were randomized to receive a single dose of 0.5 mL intramuscular injection of 20vPnC (Day 1).	
Reporting group title	Cohort 2: 13vPnC
Reporting group description:	
Subjects aged 50 through 59 years were randomized to receive a single dose of 0.5 mL intramuscular injection of 13vPnC (Day 1).	
Reporting group title	Cohort 3: 20vPnC
Reporting group description:	
Subjects aged 18 through 49 years were randomized to receive a single dose of 0.5 mL intramuscular injection of 20vPnC (Day 1).	
Reporting group title	Cohort 3: 13vPnC
Reporting group description:	
Subjects aged 18 through 49 years were randomized to receive a single dose of 0.5 mL intramuscular injection of 13vPnC (Day 1).	
Subject analysis set title	Cohort 1: 20vPnC/Saline (60-64 Years of Age)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants of 60-64 years of age who were enrolled in Cohort 1, received Vaccination 1 as randomized, had at least 1 valid OPA titer from the blood collection 27 to 49 days after 20vPnC, had no other major protocol deviations.	

Primary: Percentage of Subjects With Local Reactions Within 10 Days After Vaccination in All Cohorts

End point title	Percentage of Subjects With Local Reactions Within 10 Days After Vaccination in All Cohorts[1]
End point description:	
Local reactions were recorded using an electronic diary. Local reactions included redness, swelling and pain at the injection site. Redness and swelling were measured and recorded in measuring device units. 1 measuring device unit =0.5 centimeter (cm). Redness and swelling were graded as mild (greater than [>] 2.0 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 population included all subjects who received 1 dose of any of the following: 20vPnC, 13vPnC, PPSV23 or saline and had safety follow-up after any vaccination. Here, "Number of subjects analysed" =number of subjects with any electronic diary data after 20vPnC or 13vPnC.	
End point type	Primary
End point timeframe:	
Within 10 days after 20vPnC or 13vPnC	

Notes:

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

End point values	Cohort 1: 20vPnC/Saline	Cohort 1: 13vPnC/PPSV23	Cohort 2: 20vPnC	Cohort 2: 13vPnC
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1505	1483	331	111
Units: percentage of subjects				
number (confidence interval 95%)				
Redness: Any	7.3 (6.0 to 8.7)	6.2 (5.0 to 7.6)	8.2 (5.4 to 11.6)	5.4 (2.0 to 11.4)
Redness: Mild	3.7 (2.8 to 4.8)	3.8 (2.9 to 4.9)	5.1 (3.0 to 8.1)	2.7 (0.6 to 7.7)
Redness: Moderate	2.8 (2.0 to 3.8)	2.2 (1.5 to 3.1)	2.7 (1.3 to 5.1)	2.7 (0.6 to 7.7)
Redness: Severe	0.8 (0.4 to 1.4)	0.2 (0.0 to 0.6)	0.3 (0.0 to 1.7)	0 (0.0 to 3.3)
Swelling: Any	7.5 (6.2 to 9.0)	8.0 (6.6 to 9.5)	8.8 (5.9 to 12.3)	10.8 (5.7 to 18.1)
Swelling: Mild	4.8 (3.8 to 6.0)	4.9 (3.8 to 6.1)	5.7 (3.5 to 8.8)	7.2 (3.2 to 13.7)
Swelling: Moderate	2.4 (1.7 to 3.3)	2.8 (2.0 to 3.8)	3.0 (1.5 to 5.5)	3.6 (1.0 to 9.0)
Swelling: Severe	0.3 (0.1 to 0.8)	0.3 (0.1 to 0.7)	0 (0.0 to 1.1)	0 (0.0 to 3.3)
Pain at the injection site: Any	55.4 (52.9 to 57.9)	54.1 (51.6 to 56.7)	72.5 (67.4 to 77.2)	69.4 (59.9 to 77.8)
Pain at the injection site: Mild	45.3 (42.8 to 47.9)	44.6 (42.1 to 47.2)	53.5 (47.9 to 58.9)	52.3 (42.6 to 61.8)
Pain at the injection site: Moderate	9.9 (8.4 to 11.5)	9.2 (7.7 to 10.8)	17.8 (13.9 to 22.4)	16.2 (9.9 to 24.4)
Pain at the injection site: Severe	0.2 (0.0 to 0.6)	0.3 (0.1 to 0.8)	1.2 (0.3 to 3.1)	0.9 (0.0 to 4.9)

End point values	Cohort 3: 20vPnC	Cohort 3: 13vPnC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	335	112		
Units: percentage of subjects				
number (confidence interval 95%)				
Redness: Any	9.0 (6.1 to 12.5)	9.8 (5.0 to 16.9)		
Redness: Mild	3.0 (1.4 to 5.4)	5.4 (2.0 to 11.3)		
Redness: Moderate	5.4 (3.2 to 8.4)	4.5 (1.5 to 10.1)		
Redness: Severe	0.6 (0.1 to 2.1)	0 (0.0 to 3.2)		
Swelling: Any	11.6 (8.4 to 15.6)	12.5 (7.0 to 20.1)		
Swelling: Mild	7.2 (4.6 to 10.5)	8.9 (4.4 to 15.8)		
Swelling: Moderate	4.5 (2.5 to 7.3)	3.6 (1.0 to 8.9)		
Swelling: Severe	0 (0.0 to 1.1)	0 (0.0 to 3.2)		
Pain at the injection site: Any	81.2 (76.6 to 85.2)	82.1 (73.8 to 88.7)		
Pain at the injection site: Mild	42.7 (37.3 to 48.2)	52.7 (43.0 to 62.2)		

Pain at the injection site: Moderate	38.2 (33.0 to 43.6)	28.6 (20.4 to 37.9)		
Pain at the injection site: Severe	0.3 (0.0 to 1.7)	0.9 (0.0 to 4.9)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Systemic Events Within 7 Days After Vaccination in All Cohorts

End point title	Percentage of Subjects With Systemic Events Within 7 Days After Vaccination in All Cohorts[2]

End point description:

Systemic events fever, fatigue, headache, muscle pain and joint pain were recorded by using an electronic diary. Fever was defined as greater than or equal to (>=) 38.0 degree Celsius (C) and categorized to >=38.0 to 38.4 degree C, >38.4 to 38.9 degree C, >38.9 to 40.0 degree C and >40.0 degree C. Fatigue, headache, muscle pain and joint pain were graded as mild (did not interfere with activity), moderate (some interference with activity) and severe (prevented daily routine activity). Safety population included all subjects who received 1 dose of any of the following: 20vPnC, 13vPnC, PPSV23 or saline and had safety follow-up after any vaccination. Here, "Number of subjects analysed" =number of subjects with any electronic diary data after 20vPnC or 13vPnC.

End point type	Primary

End point timeframe:

Within 7 days after 20vPnC or 13vPnC

Notes:

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

End point values	Cohort 1: 20vPnC/Saline	Cohort 1: 13vPnC/PPSV23	Cohort 2: 20vPnC	Cohort 2: 13vPnC
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1505	1483	331	111
Units: percentage of subjects				
number (confidence interval 95%)				
Fever: >=38.0 degree C	0.9 (0.5 to 1.6)	0.8 (0.4 to 1.4)	1.5 (0.5 to 3.5)	0.9 (0.0 to 4.9)
Fever: >=38.0 degree C to 38.4 degree C	0.3 (0.1 to 0.7)	0.4 (0.1 to 0.9)	0.6 (0.1 to 2.2)	0.9 (0.0 to 4.9)
Fever: >38.4 degree C to 38.9 degree C	0.3 (0.1 to 0.7)	0.2 (0.0 to 0.6)	0.3 (0.0 to 1.7)	0 (0.0 to 3.3)
Fever: >38.9 degree C to 40.0 degree C	0.0 (0.0 to 0.4)	0 (0.0 to 0.2)	0.3 (0.0 to 1.7)	0 (0.0 to 3.3)
Fever: >40.0 degree C	0.3 (0.1 to 0.8)	0.2 (0.0 to 0.6)	0.3 (0.0 to 1.7)	0 (0.0 to 3.3)
Fatigue: Any	30.2 (27.9 to 32.6)	30.7 (28.3 to 33.1)	39.3 (34.0 to 44.8)	36.0 (27.1 to 45.7)
Fatigue: Mild	16.1 (14.3 to 18.1)	17.5 (15.6 to 19.6)	21.1 (16.9 to 25.9)	18.0 (11.4 to 26.4)
Fatigue: Moderate	12.8 (11.2 to 14.6)	11.9 (10.3 to 13.7)	17.2 (13.3 to 21.7)	15.3 (9.2 to 23.4)
Fatigue: Severe	1.2 (0.7 to 1.9)	1.2 (0.7 to 1.9)	0.9 (0.2 to 2.6)	2.7 (0.6 to 7.7)
Headache: Any	21.5 (19.5 to 23.7)	23.3 (21.1 to 25.5)	32.3 (27.3 to 37.7)	36.0 (27.1 to 45.7)
Headache: Mild	15.5 (13.7 to 17.4)	17.0 (15.1 to 19.0)	20.5 (16.3 to 25.3)	21.6 (14.4 to 30.4)
Headache: Moderate	5.4 (4.3 to 6.6)	5.9 (4.8 to 7.3)	10.9 (7.7 to 14.7)	13.5 (7.8 to 21.3)

Headache: Severe	0.7 (0.3 to 1.2)	0.3 (0.1 to 0.8)	0.9 (0.2 to 2.6)	0.9 (0.0 to 4.9)
Muscle pain: Any	39.1 (36.6 to 41.6)	37.3 (34.8 to 39.8)	49.8 (44.3 to 55.4)	49.5 (39.9 to 59.2)
Muscle pain: Mild	28.9 (26.6 to 31.3)	26.8 (24.6 to 29.2)	33.8 (28.8 to 39.2)	31.5 (23.0 to 41.0)
Muscle pain: Moderate	9.8 (8.3 to 11.4)	10.0 (8.5 to 11.6)	15.4 (11.7 to 19.8)	17.1 (10.6 to 25.4)
Muscle pain: Severe	0.4 (0.1 to 0.9)	0.5 (0.2 to 1.0)	0.6 (0.1 to 2.2)	0.9 (0.0 to 4.9)
Joint pain: Any	12.6 (11.0 to 14.4)	13.7 (12.0 to 15.5)	15.4 (11.7 to 19.8)	20.7 (13.6 to 29.5)
Joint pain: Mild	6.9 (5.7 to 8.3)	7.1 (5.9 to 8.6)	10.6 (7.5 to 14.4)	12.6 (7.1 to 20.3)
Joint pain: Moderate	5.4 (4.3 to 6.6)	6.3 (5.2 to 7.7)	4.8 (2.8 to 7.7)	7.2 (3.2 to 13.7)
Joint pain: Severe	0.3 (0.1 to 0.8)	0.2 (0.0 to 0.6)	0 (0.0 to 1.1)	0.9 (0.0 to 4.9)

End point values	Cohort 3: 20vPnC	Cohort 3: 13vPnC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	335	112		
Units: percentage of subjects				
number (confidence interval 95%)				
Fever: >=38.0 degree C	1.2 (0.3 to 3.0)	1.8 (0.2 to 6.3)		
Fever: >=38.0 degree C to 38.4 degree C	0.6 (0.1 to 2.1)	0 (0.0 to 3.2)		
Fever: >38.4 degree C to 38.9 degree C	0.3 (0.0 to 1.7)	0 (0.0 to 3.2)		
Fever: >38.9 degree C to 40.0 degree C	0.3 (0.0 to 1.7)	1.8 (0.2 to 6.3)		
Fever: >40.0 degree C	0 (0.0 to 1.1)	0 (0.0 to 3.2)		
Fatigue: Any	42.7 (37.3 to 48.2)	43.8 (34.4 to 53.4)		
Fatigue: Mild	18.8 (14.8 to 23.4)	20.5 (13.5 to 29.2)		
Fatigue: Moderate	22.1 (17.8 to 26.9)	19.6 (12.7 to 28.2)		
Fatigue: Severe	1.8 (0.7 to 3.9)	3.6 (1.0 to 8.9)		
Headache: Any	38.8 (33.6 to 44.3)	33.9 (25.3 to 43.5)		
Headache: Mild	21.5 (17.2 to 26.3)	16.1 (9.8 to 24.2)		
Headache: Moderate	14.6 (11.0 to 18.9)	17.0 (10.5 to 25.2)		
Headache: Severe	2.7 (1.2 to 5.0)	0.9 (0.0 to 4.9)		
Muscle pain: Any	66.6 (61.2 to 71.6)	74.1 (65.0 to 81.9)		
Muscle pain: Mild	36.4 (31.3 to 41.8)	42.0 (32.7 to 51.7)		
Muscle pain: Moderate	29.0 (24.2 to 34.1)	31.3 (22.8 to 40.7)		
Muscle pain: Severe	1.2 (0.3 to 3.0)	0.9 (0.0 to 4.9)		
Joint pain: Any	13.4 (10.0 to 17.6)	17.9 (11.3 to 26.2)		
Joint pain: Mild	6.3 (3.9 to 9.4)	8.9 (4.4 to 15.8)		
Joint pain: Moderate	7.2 (4.6 to 10.5)	8.0 (3.7 to 14.7)		
Joint pain: Severe	0 (0.0 to 1.1)	0.9 (0.0 to 4.9)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Adverse Events (AEs) Within 1 Month After Vaccination in All Cohorts

End point title	Percentage of Subjects With Adverse Events (AEs) Within 1 Month After Vaccination in All Cohorts[3]

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. Safety population included all subjects who received 1 dose of any of the following: 20vPnC, 13vPnC, PPSV23 or saline and had safety follow-up after any vaccination.

End point type	Primary

End point timeframe:

Within 1 month after 20vPnC or 13vPnC

Notes:

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

End point values	Cohort 1: 20vPnC/Saline	Cohort 1: 13vPnC/PPSV23	Cohort 2: 20vPnC	Cohort 2: 13vPnC
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1507	1490	334	111
Units: percentage of subjects				
number (confidence interval 95%)	9.8 (8.4 to 11.4)	11.1 (9.6 to 12.8)	10.2 (7.2 to 13.9)	8.1 (3.8 to 14.8)

End point values	Cohort 3: 20vPnC	Cohort 3: 13vPnC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	335	112		
Units: percentage of subjects				
number (confidence interval 95%)	15.2 (11.6 to 19.5)	11.6 (6.3 to 19.0)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Serious Adverse Events (SAEs) Within 6

Months After Vaccination in All Cohorts

End point title	Percentage of Subjects With Serious Adverse Events (SAEs) Within 6 Months After Vaccination in All Cohorts[4]

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 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 or that is considered to be an important medical event. Safety population included all subjects who received 1 dose of any of the following: 20vPnC, 13vPnC, PPSV23 or saline and had safety follow-up after any vaccination.

End point type	Primary

End point timeframe:

Within 6 months after 20vPnC or 13vPnC

Notes:

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

End point values	Cohort 1: 20vPnC/Saline	Cohort 1: 13vPnC/PPSV23	Cohort 2: 20vPnC	Cohort 2: 13vPnC
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1507	1490	334	111
Units: percentage of subjects				
number (confidence interval 95%)	2.4 (1.7 to 3.3)	1.9 (1.3 to 2.8)	0.3 (0.0 to 1.7)	0.9 (0.0 to 4.9)

End point values	Cohort 3: 20vPnC	Cohort 3: 13vPnC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	335	112		
Units: percentage of subjects				
number (confidence interval 95%)	0.6 (0.1 to 2.1)	0.9 (0.0 to 4.9)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Newly Diagnosed Chronic Medical Conditions (NDCMCs) Within 6 Months After Vaccination in All Cohorts

End point title	Percentage of Subjects With Newly Diagnosed Chronic Medical Conditions (NDCMCs) Within 6 Months After Vaccination in All Cohorts[5]

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. Safety population included all subjects who received 1 dose of any of the following: 20vPnC, 13vPnC, PPSV23 or saline and had safety follow-up after any vaccination.

End point type	Primary

End point timeframe:

Within 6 months after 20vPnC or 13vPnC

Notes:

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

End point values	Cohort 1: 20vPnC/Saline	Cohort 1: 13vPnC/PPSV23	Cohort 2: 20vPnC	Cohort 2: 13vPnC
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1507	1490	334	111
Units: percentage of subjects				
number (confidence interval 95%)	2.3 (1.6 to 3.1)	2.3 (1.6 to 3.3)	1.5 (0.5 to 3.5)	0.9 (0.0 to 4.9)

End point values	Cohort 3: 20vPnC	Cohort 3: 13vPnC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	335	112		
Units: percentage of subjects				
number (confidence interval 95%)	1.5 (0.5 to 3.4)	1.8 (0.2 to 6.3)		

Statistical analyses

No statistical analyses for this end point

Primary: Pneumococcal Opsonophagocytic Activity (OPA) Geometric Mean Titers (GMTs) for the 13 Matched Serotypes at 1 Month After Vaccination 1 (20vPnC or 13vPnC) in Cohort 1: Evaluable 13-Matched Immunogenicity Population

End point title	Pneumococcal Opsonophagocytic Activity (OPA) Geometric Mean Titers (GMTs) for the 13 Matched Serotypes at 1 Month After Vaccination 1 (20vPnC or 13vPnC) in Cohort 1: Evaluable 13-Matched Immunogenicity Population[6]

End point description:

OPA GMTs were determined for serotypes: 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F and 23F. OPA titer was expressed as reciprocal of the highest serum dilution. OPA geometric mean and 2-sided 95% CIs were calculated. Evaluable 13-matched immunogenicity population included subjects who were enrolled in the appropriate cohort based on age, received Vaccination 1 as randomized, had at least 1 valid OPA titer for any of the 13 matched serotypes from the blood collection 27 to 49 days after Vaccination 1, had no other major protocol deviations. Here, "n" =subjects evaluable for this endpoint at specified rows.

End point type	Primary

End point timeframe:

1 month after Vaccination 1

Notes:

[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 for reporting arms “Cohort 1: 20vPnC/Saline” and “Cohort 1: 13vPnC/PPSV23” only.

End point values	Cohort 1: 20vPnC/Saline	Cohort 1: 13vPnC/PPSV23		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1435	1420		
Units: titer				
geometric mean (confidence interval 95%)				
Serotype 1 (n =1430, 1419)	123.4 (112.3 to 135.5)	153.8 (140.2 to 168.8)		
Serotype 3 (n =1415, 1411)	40.7 (38.0 to 43.6)	47.8 (44.7 to 51.2)		
Serotype 4 (n =1415, 1409)	508.7 (456.5 to 566.9)	626.9 (563.5 to 697.4)		
Serotype 5 (n =1418, 1395)	91.6 (83.4 to 100.5)	109.7 (100.1 to 120.3)		
Serotype 6A (n =1403, 1390)	889.0 (795.0 to 994.1)	1165.1 (1043.3 to 1301.0)		
Serotype 6B (n =1413, 1401)	1115.2 (1003.1 to 1239.8)	1341.3 (1208.5 to 1488.8)		
Serotype 7F (n =1409, 1391)	968.8 (887.0 to 1058.3)	1129.2 (1034.7 to 1232.4)		
Serotype 9V (n =1399, 1391)	1455.5 (1317.5 to 1608.0)	1567.8 (1420.5 to 1730.5)		
Serotype 14 (n =1418, 1408)	746.7 (679.0 to 821.2)	746.7 (679.8 to 820.1)		
Serotype 18C (n =1420, 1403)	1252.6 (1123.1 to 1397.0)	1482.3 (1330.5 to 1651.5)		
Serotype 19A (n =1420, 1398)	517.9 (472.2 to 568.0)	645.3 (588.9 to 707.1)		
Serotype 19F (n =1421, 1403)	265.8 (240.2 to 294.1)	333.3 (301.5 to 368.3)		
Serotype 23F (n =1424, 1409)	276.5 (242.5 to 315.2)	335.1 (294.4 to 381.4)		

Statistical analyses

Statistical analysis title	NI of 20vPnC to 13vPnC for 13 matched serotypes
Statistical analysis description:	
Serotype 1: Geometric mean ratio (20vPnC/Saline vs 13vPnC/PPSV23) and the 2-sided 95% CI	
Comparison groups	Cohort 1: 20vPnC/Saline v Cohort 1: 13vPnC/PPSV23
Number of subjects included in analysis	2855
Analysis specification	Pre-specified
Analysis type	non-inferiority[7]
Parameter estimate	Ratio of GMTs
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	0.9

Notes:

[7] - Noninferiority for a serotype was declared if the lower bound of the 2-sided 95% CI for the geometric mean ratio (GMR) for that serotype was greater than 0.5 (2-fold criterion).

Statistical analysis title	NI of 20vPnC to 13vPnC for 13 matched serotypes

Statistical analysis description:

Serotype 3: Geometric mean ratio (20vPnC/Saline vs 13vPnC/PPSV23) and the 2-sided 95% CI

Comparison groups	Cohort 1: 20vPnC/Saline v Cohort 1: 13vPnC/PPSV23
Number of subjects included in analysis	2855
Analysis specification	Pre-specified
Analysis type	non-inferiority[8]
Parameter estimate	Ratio of GMTs
Point estimate	0.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.78
upper limit	0.93

Notes:

[8] - Noninferiority for a serotype was declared if the lower bound of the 2-sided 95% CI for the GMR for that serotype was greater than 0.5 (2-fold criterion).

Statistical analysis title	NI of 20vPnC to 13vPnC for 13 matched serotypes

Statistical analysis description:

Serotype 4: Geometric mean ratio (20vPnC/Saline vs 13vPnC/PPSV23) and the 2-sided 95% CI

Comparison groups	Cohort 1: 20vPnC/Saline v Cohort 1: 13vPnC/PPSV23
Number of subjects included in analysis	2855
Analysis specification	Pre-specified
Analysis type	non-inferiority[9]
Parameter estimate	Ratio of GMTs
Point estimate	0.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	0.93

Notes:

[9] - Noninferiority for a serotype was declared if the lower bound of the 2-sided 95% CI for the GMR for that serotype was greater than 0.5 (2-fold criterion).

Statistical analysis title	NI of 20vPnC to 13vPnC for 13 matched serotypes

Statistical analysis description:

Serotype 5: Geometric mean ratio (20vPnC/Saline vs 13vPnC/PPSV23) and the 2-sided 95% CI

Comparison groups	Cohort 1: 20vPnC/Saline v Cohort 1: 13vPnC/PPSV23
Number of subjects included in analysis	2855
Analysis specification	Pre-specified
Analysis type	non-inferiority[10]
Parameter estimate	Ratio of GMTs
Point estimate	0.83

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.74
upper limit	0.94

Notes:

[10] - Noninferiority for a serotype was declared if the lower bound of the 2-sided 95% CI for the GMR for that serotype was greater than 0.5 (2-fold criterion).

Statistical analysis title	NI of 20vPnC to 13vPnC for 13 matched serotypes

Statistical analysis description:

Serotype 6A: Geometric mean ratio (20vPnC/Saline vs 13vPnC/PPSV23) and the 2-sided 95% CI

Comparison groups	Cohort 1: 20vPnC/Saline v Cohort 1: 13vPnC/PPSV23
Number of subjects included in analysis	2855
Analysis specification	Pre-specified
Analysis type	non-inferiority[11]
Parameter estimate	Ratio of GMTs
Point estimate	0.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.66
upper limit	0.88

Notes:

[11] - Noninferiority for a serotype was declared if the lower bound of the 2-sided 95% CI for the GMR for that serotype was greater than 0.5 (2-fold criterion).

Statistical analysis title	NI of 20vPnC to 13vPnC for 13 matched serotypes

Statistical analysis description:

Serotype 6B: Geometric mean ratio (ratio of GMTs 20vPnC to 13vPnC) and 2-sided CIs were calculated by exponentiating the difference of LS means and the corresponding CIs based on a regression model with vaccine group, sex, smoking status, age at vaccination in years (continuous), and baseline log transformed OPA titers.

Comparison groups	Cohort 1: 20vPnC/Saline v Cohort 1: 13vPnC/PPSV23
Number of subjects included in analysis	2855
Analysis specification	Pre-specified
Analysis type	non-inferiority[12]
Parameter estimate	Ratio of GMTs
Point estimate	0.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.73
upper limit	0.95

Notes:

[12] - Noninferiority for a serotype was declared if the lower bound of the 2-sided 95% CI for the GMR for that serotype was greater than 0.5 (2-fold criterion).

Statistical analysis title	NI of 20vPnC to 13vPnC for 13 matched serotypes

Statistical analysis description:

Serotype 7F: Geometric mean ratio (20vPnC/Saline vs 13vPnC/PPSV23) and the 2-sided 95% CI

Comparison groups	Cohort 1: 20vPnC/Saline v Cohort 1: 13vPnC/PPSV23

Number of subjects included in analysis	2855
Analysis specification	Pre-specified
Analysis type	non-inferiority[13]
Parameter estimate	Ratio of GMTs
Point estimate	0.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.77
upper limit	0.96

Notes:

[13] - Noninferiority for a serotype was declared if the lower bound of the 2-sided 95% CI for the GMR for that serotype was greater than 0.5 (2-fold criterion).

Statistical analysis title	NI of 20vPnC to 13vPnC for 13 matched serotypes

Statistical analysis description:

Serotype 9V: Geometric mean ratio (20vPnC/Saline vs 13vPnC/PPSV23) and the 2-sided 95% CI

Comparison groups	Cohort 1: 20vPnC/Saline v Cohort 1: 13vPnC/PPSV23
Number of subjects included in analysis	2855
Analysis specification	Pre-specified
Analysis type	non-inferiority[14]
Parameter estimate	Ratio of GMTs
Point estimate	0.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.82
upper limit	1.05

Notes:

[14] - Noninferiority for a serotype was declared if the lower bound of the 2-sided 95% CI for the GMR for that serotype was greater than 0.5 (2-fold criterion).

Statistical analysis title	NI of 20vPnC to 13vPnC for 13 Matched Serotypes

Statistical analysis description:

Serotype 14: Geometric mean ratio (20vPnC/Saline vs 13vPnC/PPSV23) and the 2-sided 95% CI

Comparison groups	Cohort 1: 20vPnC/Saline v Cohort 1: 13vPnC/PPSV23
Number of subjects included in analysis	2855
Analysis specification	Pre-specified
Analysis type	non-inferiority[15]
Parameter estimate	Ratio of GMTs
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.89
upper limit	1.13

Notes:

[15] - Noninferiority for a serotype was declared if the lower bound of the 2-sided 95% CI for the GMR for that serotype was greater than 0.5 (2-fold criterion).

Statistical analysis title	NI of 20vPnC to 13vPnC for 13 Matched Serotypes

Statistical analysis description:

Serotype 18C: Geometric mean ratio (20vPnC/Saline vs 13vPnC/PPSV23) and the 2-sided 95% CI

Comparison groups	Cohort 1: 20vPnC/Saline v Cohort 1: 13vPnC/PPSV23
Number of subjects included in analysis	2855
Analysis specification	Pre-specified
Analysis type	non-inferiority[16]
Parameter estimate	Ratio of GMTs
Point estimate	0.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.74
upper limit	0.97

Notes:

[16] - Noninferiority for a serotype was declared if the lower bound of the 2-sided 95% CI for the GMR for that serotype was greater than 0.5 (2-fold criterion).

Statistical analysis title	NI of 20vPnC to 13vPnC for 13 Matched Serotypes

Statistical analysis description:

Serotype 19A: Geometric mean ratio (20vPnC/Saline vs 13vPnC/PPSV23) and the 2-sided 95% CI

Comparison groups	Cohort 1: 20vPnC/Saline v Cohort 1: 13vPnC/PPSV23
Number of subjects included in analysis	2855
Analysis specification	Pre-specified
Analysis type	non-inferiority[17]
Parameter estimate	Ratio of GMTs
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	0.9

Notes:

[17] - Noninferiority for a serotype was declared if the lower bound of the 2-sided 95% CI for the GMR for that serotype was greater than 0.5 (2-fold criterion).

Statistical analysis title	NI of 20vPnC to 13vPnC for 13 Matched Serotypes

Statistical analysis description:

Serotype 19F: Geometric mean ratio (20vPnC/Saline vs 13vPnC/PPSV23) and the 2-sided 95% CI

Comparison groups	Cohort 1: 20vPnC/Saline v Cohort 1: 13vPnC/PPSV23
Number of subjects included in analysis	2855
Analysis specification	Pre-specified
Analysis type	non-inferiority[18]
Parameter estimate	Ratio of GMTs
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	0.91

Notes:

[18] - Noninferiority for a serotype was declared if the lower bound of the 2-sided 95% CI for the GMR for that serotype was greater than 0.5 (2-fold criterion).

Statistical analysis title	NI of 20vPnC to 13vPnC for 13 Matched Serotypes

Statistical analysis description:	
Serotype 23F: Geometric mean ratio (20vPnC/Saline vs 13vPnC/PPSV23) and the 2-sided 95% CI	
Comparison groups	Cohort 1: 20vPnC/Saline v Cohort 1: 13vPnC/PPSV23
Number of subjects included in analysis	2855
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Ratio of GMTs
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	0.91

Primary: Pneumococcal OPA GMTs for the 7 Additional Serotypes at 1 Month After Vaccination 1 (20vPnC) or 1 Month After Vaccination 2 (PPSV23) in Cohort 1: Evaluable 7-Additional Immunogenicity Population (E7-AIP)

End point title	Pneumococcal OPA GMTs for the 7 Additional Serotypes at 1 Month After Vaccination 1 (20vPnC) or 1 Month After Vaccination 2 (PPSV23) in Cohort 1: Evaluable 7-Additional Immunogenicity Population (E7-AIP)[19]

End point description:

OPA GMTs were determined for serotypes: 8, 10A, 11A, 12F, 15B, 22F and 33F. OPA titer was expressed as reciprocal of the highest serum dilution. OPA geometric mean and 2-sided 95% CIs were calculated. Evaluable 7-additional immunogenicity population: subjects who were enrolled in the appropriate cohort based on age, received 20vPnC if randomized to 20vPnC/saline group or received both vaccinations if randomized to 13vPnC/PPSV23 group, had at least 1 valid OPA titers for any of the 7 additional serotypes from the blood collection 27 to 49 days after Vaccination 1 or Vaccination 2 respectively, had no other major protocol deviations. Here, 'n' =subjects evaluable at specified rows.

End point type	Primary

End point timeframe:

1 month after Vaccination 1 in “Cohort 1: 20vPnC/Saline”; 1 month after Vaccination 2 in “Cohort 1: 13vPnC/PPSV23”

Notes:

[19] - 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 for reporting arms “Cohort 1: 20vPnC/Saline” and “Cohort 1: 13vPnC/PPSV23” only.

End point values	Cohort 1: 20vPnC/Saline	Cohort 1: 13vPnC/PPSV23		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1433	1383		
Units: titer				
geometric mean (confidence interval 95%)				
Serotype 8 (n =1374, 1319)	465.6 (422.5 to 513.1)	848.1 (769.1 to 935.2)		
Serotype 10A (n =1310, 1263)	2007.6 (1808.0 to 2229.1)	1079.9 (972.1 to 1199.7)		
Serotype 11A (n =1198, 1209)	4426.8 (3965.5 to 4941.8)	2534.9 (2276.8 to 2822.3)		

Serotype 12F (n =1294, 1222)	2538.7 (2255.3 to 2857.7)	1716.6 (1521.8 to 1936.3)		
Serotype 15B (n =1283, 1249)	2398.2 (2090.6 to 2751.2)	768.5 (669.7 to 881.9)		
Serotype 22F (n =1274, 1227)	3666.2 (3244.4 to 4143.0)	1846.2 (1636.6 to 2082.6)		
Serotype 33F (n =1157, 1201)	5125.9 (4611.3 to 5698.0)	3720.6 (3356.2 to 4124.6)		

Statistical analyses

Statistical analysis title	NI of 20vPnC to PPSV23 for 7 Additional Serotypes
Statistical analysis description:	
Serotype 8: Geometric mean ratio (20vPnC/Saline vs 13vPnC/PPSV23) and the 2-sided 95% CI	
Comparison groups	Cohort 1: 20vPnC/Saline v Cohort 1: 13vPnC/PPSV23
Number of subjects included in analysis	2816
Analysis specification	Pre-specified
Analysis type	non-inferiority[20]
Parameter estimate	Ratio of GMTs
Point estimate	0.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.49
upper limit	0.62

Notes:

[20] - Noninferiority for a serotype was declared if the lower bound of the 2-sided 95% CI for the GMR for that serotype was greater than 0.5 (2-fold criterion).

Statistical analysis title	NI of 20vPnC to PPSV23 for 7 Additional Serotypes
Statistical analysis description:	
Serotype 10A: Geometric mean ratio (20vPnC/Saline vs 13vPnC/PPSV23) and the 2-sided 95% CI	
Comparison groups	Cohort 1: 20vPnC/Saline v Cohort 1: 13vPnC/PPSV23
Number of subjects included in analysis	2816
Analysis specification	Pre-specified
Analysis type	non-inferiority[21]
Parameter estimate	Ratio of GMTs
Point estimate	1.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.63
upper limit	2.12

Notes:

[21] - Noninferiority for a serotype was declared if the lower bound of the 2-sided 95% CI for the GMR for that serotype was greater than 0.5 (2-fold criterion).

Statistical analysis title	NI of 20vPnC to PPSV23 for 7 Additional Serotypes

Statistical analysis description:	
Serotype 11A: Geometric mean ratio (20vPnC/Saline vs 13vPnC/PPSV23) and the 2-sided 95% CI	
Comparison groups	Cohort 1: 20vPnC/Saline v Cohort 1: 13vPnC/PPSV23
Number of subjects included in analysis	2816
Analysis specification	Pre-specified
Analysis type	non-inferiority[22]
Parameter estimate	Ratio of GMTs
Point estimate	1.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.52
upper limit	2.01

Notes:

[22] - Noninferiority for a serotype was declared if the lower bound of the 2-sided 95% CI for the GMR for that serotype was greater than 0.5 (2-fold criterion).

Statistical analysis title	NI of 20vPnC to PPSV23 for 7 Additional Serotypes
Statistical analysis description:	
Serotype 12F: Geometric mean ratio (20vPnC/Saline vs 13vPnC/PPSV23) and the 2-sided 95% CI	
Comparison groups	Cohort 1: 20vPnC/Saline v Cohort 1: 13vPnC/PPSV23
Number of subjects included in analysis	2816
Analysis specification	Pre-specified
Analysis type	non-inferiority[23]
Parameter estimate	Ratio of GMTs
Point estimate	1.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.27
upper limit	1.72

Notes:

[23] - Noninferiority for a serotype was declared if the lower bound of the 2-sided 95% CI for the GMR for that serotype was greater than 0.5 (2-fold criterion).

Statistical analysis title	NI of 20vPnC to PPSV23 for 7 Additional Serotypes
Statistical analysis description:	
Serotype 15B: Geometric mean ratio (20vPnC/Saline vs 13vPnC/PPSV23) and the 2-sided 95% CI	
Comparison groups	Cohort 1: 20vPnC/Saline v Cohort 1: 13vPnC/PPSV23
Number of subjects included in analysis	2816
Analysis specification	Pre-specified
Analysis type	non-inferiority[24]
Parameter estimate	Ratio of GMTs
Point estimate	3.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.62
upper limit	3.71

Notes:

[24] - Noninferiority for a serotype was declared if the lower bound of the 2-sided 95% CI for the GMR for that serotype was greater than 0.5 (2-fold criterion).

Statistical analysis title	NI of 20vPnC to PPSV23 for 7 Additional Serotypes

Statistical analysis description:

Serotype 22F: Geometric mean ratio (20vPnC/Saline vs 13vPnC/PPSV23) and the 2-sided 95% CI

Comparison groups	Cohort 1: 20vPnC/Saline v Cohort 1: 13vPnC/PPSV23
Number of subjects included in analysis	2816
Analysis specification	Pre-specified
Analysis type	non-inferiority[25]
Parameter estimate	Ratio of GMTs
Point estimate	1.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.7
upper limit	2.32

Notes:

[25] - Noninferiority for a serotype was declared if the lower bound of the 2-sided 95% CI for the GMR for that serotype was greater than 0.5 (2-fold criterion).

Statistical analysis title	NI of 20vPnC to PPSV23 for 7 Additional Serotypes

Statistical analysis description:

Serotype 33F: Geometric mean ratio (20vPnC/Saline vs 13vPnC/PPSV23) and the 2-sided 95% CI

Comparison groups	Cohort 1: 20vPnC/Saline v Cohort 1: 13vPnC/PPSV23
Number of subjects included in analysis	2816
Analysis specification	Pre-specified
Analysis type	non-inferiority[26]
Parameter estimate	Ratio of GMTs
Point estimate	1.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.21
upper limit	1.57

Notes:

[26] - Noninferiority for a serotype was declared if the lower bound of the 2-sided 95% CI for the GMR for that serotype was greater than 0.5 (2-fold criterion).

Secondary: Pneumococcal OPA GMTs for the 20 Vaccines Serotypes at 1 Month After 20vPnC Vaccination in Cohort 2, 50 Through 59 Years of Age and Cohort 1, Only 60 Through 64 Years of Age: Evaluable-20 Immunogenicity Population

End point title	Pneumococcal OPA GMTs for the 20 Vaccines Serotypes at 1 Month After 20vPnC Vaccination in Cohort 2, 50 Through 59 Years of Age and Cohort 1, Only 60 Through 64 Years of Age: Evaluable-20 Immunogenicity Population[27]

End point description:

OPA GMTs were determined for serotypes: 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F, 8, 10A, 11A, 12F, 15B, 22F and 33F. OPA titer was expressed as reciprocal of the highest serum dilution. OPA geometric mean and 2-sided 95% CIs were calculated. Evaluable-20 immunogenicity population included subjects who were enrolled in the appropriate cohort based on age, received the vaccination as randomized, had at least 1 valid OPA titer from the blood collection 27 to 49 days after 20vPnC, had no other major protocol deviations. Here, "n" =subjects evaluable for this endpoint at specified rows.

End point type	Secondary

End point timeframe:

1 month after vaccination

Notes:

[27] - 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 for reporting arms "Cohort 1: 20vPnC/Saline" and "Cohort 1: 13vPnC/PPSV23" only.

End point values	Cohort 2: 20vPnC	Cohort 1: 20vPnC/Saline (60-64 Years of Age)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	321	946		
Units: titer				
geometric mean (confidence interval 95%)				
Serotype 1 (n =320, 941)	135.9 (113.1 to 163.4)	131.8 (117.2 to 148.3)		
Serotype 3 (n =318, 935)	43.3 (38.0 to 49.4)	40.9 (37.6 to 44.5)		
Serotype 4 (n =318, 931)	633.3 (513.9 to 780.4)	577.9 (505.5 to 660.6)		
Serotype 5 (n =313, 935)	84.6 (70.3 to 101.8)	96.5 (85.8 to 108.6)		
Serotype 6A (n =318, 921)	1203.9 (968.1 to 1497.1)	997.1 (866.5 to 1147.5)		
Serotype 6B (n =318, 933)	1502.7 (1228.2 to 1838.5)	1199.0 (1054.3 to 1363.4)		
Serotype 7F (n =313, 924)	1047.0 (884.0 to 1240.2)	1173.0 (1052.9 to 1306.9)		
Serotype 9V (n =312, 922)	1725.7 (1424.4 to 2090.6)	1687.9 (1493.7 to 1907.3)		
Serotype 14 (n =313, 933)	926.2 (761.8 to 1126.0)	742.3 (655.8 to 840.2)		
Serotype 18C (n =315, 937)	1805.0 (1459.6 to 2232.2)	1355.2 (1184.3 to 1550.7)		
Serotype 19A (n =318, 932)	618.4 (519.9 to 735.5)	600.3 (537.5 to 670.6)		
Serotype 19F (n =320, 937)	286.7 (236.0 to 348.2)	290.4 (256.4 to 329.0)		
Serotype 23F (n =319, 937)	549.1 (425.4 to 708.9)	327.5 (278.2 to 385.6)		
Serotype 8 (n =314, 901)	486.9 (400.6 to 591.9)	502.3 (442.8 to 569.8)		
Serotype 10A (n =296, 857)	2520.4 (2076.0 to 3060.0)	2437.0 (2149.8 to 2762.5)		
Serotype 11A (n =271, 796)	6416.9 (5131.9 to 8023.6)	5248.9 (4564.5 to 6035.9)		
Serotype 12F (n =292, 855)	3445.1 (2807.8 to 4227.1)	3105.2 (2722.7 to 3541.4)		
Serotype 15B (n =284, 830)	3355.9 (2582.0 to 4361.8)	2873.7 (2438.1 to 3387.1)		
Serotype 22F (n =284, 835)	3808.1 (2998.2 to 4836.8)	4228.4 (3629.6 to 4926.0)		

Serotype 33F (n =266, 765)	5571.3 (4495.7 to 6904.2)	5445.2 (4749.2 to 6243.2)		

Statistical analyses

Statistical analysis title	NI of Cohort 2 to Cohort 1 (60-64 yrs)
Statistical analysis description:	
Serotype 1: GMR (20vPnC Cohort 2 vs 20vPnC Cohort 1 60-64 years of age) and the 2-sided 95% CI	
Comparison groups	Cohort 2: 20vPnC v Cohort 1: 20vPnC/Saline (60-64 Years of Age)
Number of subjects included in analysis	1267
Analysis specification	Pre-specified
Analysis type	non-inferiority[28]
Parameter estimate	Ratio of GMTs
Point estimate	1.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.84
upper limit	1.26

Notes:

[28] - Noninferiority for a serotype was declared if the lower bound of the 2-sided 95% CI for the GMR for that serotype was greater than 0.5 (2-fold criterion).

Statistical analysis title	NI of Cohort 2 to Cohort 1 (60-64 yrs)
Statistical analysis description:	
Serotype 3: GMR (20vPnC Cohort 2 vs 20vPnC Cohort 1 60-64 years of age) and the 2-sided 95% CI	
Comparison groups	Cohort 2: 20vPnC v Cohort 1: 20vPnC/Saline (60-64 Years of Age)
Number of subjects included in analysis	1267
Analysis specification	Pre-specified
Analysis type	non-inferiority[29]
Parameter estimate	Ratio of GMTs
Point estimate	1.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.92
upper limit	1.22

Notes:

[29] - Noninferiority for a serotype was declared if the lower bound of the 2-sided 95% CI for the GMR for that serotype was greater than 0.5 (2-fold criterion).

Statistical analysis title	NI of Cohort 2 to Cohort 1 (60-64 yrs)
Statistical analysis description:	
Serotype 4: GMR (20vPnC Cohort 2 vs 20vPnC Cohort 1 60-64 years of age) and the 2-sided 95% CI	
Comparison groups	Cohort 2: 20vPnC v Cohort 1: 20vPnC/Saline (60-64 Years of Age)

Number of subjects included in analysis	1267
Analysis specification	Pre-specified
Analysis type	non-inferiority[30]
Parameter estimate	Ratio of GMTs
Point estimate	1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.87
upper limit	1.38

Notes:

[30] - Noninferiority for a serotype was declared if the lower bound of the 2-sided 95% CI for the GMR for that serotype was greater than 0.5 (2-fold criterion).

Statistical analysis title	NI of Cohort 2 to Cohort 1 (60-64 yrs)

Statistical analysis description:

Serotype 5: GMR (20vPnC Cohort 2 vs 20vPnC Cohort 1 60-64 years of age) and the 2-sided 95% CI

Comparison groups	Cohort 2: 20vPnC v Cohort 1: 20vPnC/Saline (60-64 Years of Age)
Number of subjects included in analysis	1267
Analysis specification	Pre-specified
Analysis type	non-inferiority[31]
Parameter estimate	Ratio of GMTs
Point estimate	0.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.72
upper limit	1.07

Notes:

[31] - Noninferiority for a serotype was declared if the lower bound of the 2-sided 95% CI for the GMR for that serotype was greater than 0.5 (2-fold criterion).

Statistical analysis title	NI of Cohort 2 to Cohort 1 (60-64 yrs)

Statistical analysis description:

Serotype 6A: GMR (20vPnC Cohort 2 vs 20vPnC Cohort 1 60-64 years of age) and the 2-sided 95% CI

Comparison groups	Cohort 2: 20vPnC v Cohort 1: 20vPnC/Saline (60-64 Years of Age)
Number of subjects included in analysis	1267
Analysis specification	Pre-specified
Analysis type	non-inferiority[32]
Parameter estimate	Ratio of GMTs
Point estimate	1.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.95
upper limit	1.53

Notes:

[32] - Noninferiority for a serotype was declared if the lower bound of the 2-sided 95% CI for the GMR for that serotype was greater than 0.5 (2-fold criterion).

Statistical analysis title	NI of Cohort 2 to Cohort 1 (60-64 yrs)

Statistical analysis description:

Serotype 6B: GMR (20vPnC Cohort 2 vs 20vPnC Cohort 1 60-64 years of age) and the 2-sided 95% CI

Comparison groups	Cohort 2: 20vPnC v Cohort 1: 20vPnC/Saline (60-64 Years of Age)
Number of subjects included in analysis	1267
Analysis specification	Pre-specified
Analysis type	non-inferiority[33]
Parameter estimate	Ratio of GMTs
Point estimate	1.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	1
upper limit	1.56

Notes:

[33] - Noninferiority for a serotype was declared if the lower bound of the 2-sided 95% CI for the GMR for that serotype was greater than 0.5 (2-fold criterion).

Statistical analysis title	NI of Cohort 2 to Cohort 1 (60-64 yrs)

Statistical analysis description:

Serotype 7F: GMR (20vPnC Cohort 2 vs 20vPnC Cohort 1 60-64 years of age) and the 2-sided 95% CI

Comparison groups	Cohort 2: 20vPnC v Cohort 1: 20vPnC/Saline (60-64 Years of Age)
Number of subjects included in analysis	1267
Analysis specification	Pre-specified
Analysis type	non-inferiority[34]
Parameter estimate	Ratio of GMTs
Point estimate	0.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.74
upper limit	1.07

Notes:

[34] - Noninferiority for a serotype was declared if the lower bound of the 2-sided 95% CI for the GMR for that serotype was greater than 0.5 (2-fold criterion).

Statistical analysis title	NI of Cohort 2 to Cohort 1 (60-64 yrs)

Statistical analysis description:

Serotype 9V: GMR (20vPnC Cohort 2 vs 20vPnC Cohort 1 60-64 years of age) and the 2-sided 95% CI

Comparison groups	Cohort 2: 20vPnC v Cohort 1: 20vPnC/Saline (60-64 Years of Age)
Number of subjects included in analysis	1267
Analysis specification	Pre-specified
Analysis type	non-inferiority[35]
Parameter estimate	Ratio of GMTs
Point estimate	1.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.83
upper limit	1.26

Notes:

[35] - Noninferiority for a serotype was declared if the lower bound of the 2-sided 95% CI for the GMR for that serotype was greater than 0.5 (2-fold criterion).

Statistical analysis title	NI of Cohort 2 to Cohort 1 (60-64 yrs)

Statistical analysis description:

Serotype 14: GMR (20vPnC Cohort 2 vs 20vPnC Cohort 1 60-64 years of age) and the 2-sided 95% CI

Comparison groups	Cohort 2: 20vPnC v Cohort 1: 20vPnC/Saline (60-64 Years of Age)
Number of subjects included in analysis	1267
Analysis specification	Pre-specified
Analysis type	non-inferiority[36]
Parameter estimate	Ratio of GMTs
Point estimate	1.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.01
upper limit	1.54

Notes:

[36] - Noninferiority for a serotype was declared if the lower bound of the 2-sided 95% CI for the GMR for that serotype was greater than 0.5 (2-fold criterion).

Statistical analysis title	NI of Cohort 2 to Cohort 1 (60-64 yrs)

Statistical analysis description:

Serotype 18C: GMR (20vPnC Cohort 2 vs 20vPnC Cohort 1 60-64 years of age) and the 2-sided 95% CI

Comparison groups	Cohort 2: 20vPnC v Cohort 1: 20vPnC/Saline (60-64 Years of Age)
Number of subjects included in analysis	1267
Analysis specification	Pre-specified
Analysis type	non-inferiority[37]
Parameter estimate	Ratio of GMTs
Point estimate	1.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.06
upper limit	1.68

Notes:

[37] - Noninferiority for a serotype was declared if the lower bound of the 2-sided 95% CI for the GMR for that serotype was greater than 0.5 (2-fold criterion).

Statistical analysis title	NI of Cohort 2 to Cohort 1 (60-64 yrs)

Statistical analysis description:

Serotype 19A: GMR (20vPnC Cohort 2 vs 20vPnC Cohort 1 60-64 years of age) and the 2-sided 95% CI

Comparison groups	Cohort 2: 20vPnC v Cohort 1: 20vPnC/Saline (60-64 Years of Age)
Number of subjects included in analysis	1267
Analysis specification	Pre-specified
Analysis type	non-inferiority[38]
Parameter estimate	Ratio of GMTs
Point estimate	1.03

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.85
upper limit	1.25

Notes:

[38] - Noninferiority for a serotype was declared if the lower bound of the 2-sided 95% CI for the GMR for that serotype was greater than 0.5 (2-fold criterion).

Statistical analysis title	NI of Cohort 2 to Cohort 1 (60-64 yrs)

Statistical analysis description:

Serotype 19F: GMR (20vPnC Cohort 2 vs 20vPnC Cohort 1 60-64 years of age) and the 2-sided 95% CI

Comparison groups	Cohort 2: 20vPnC v Cohort 1: 20vPnC/Saline (60-64 Years of Age)
Number of subjects included in analysis	1267
Analysis specification	Pre-specified
Analysis type	non-inferiority[39]
Parameter estimate	Ratio of GMTs
Point estimate	0.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8
upper limit	1.22

Notes:

[39] - Noninferiority for a serotype was declared if the lower bound of the 2-sided 95% CI for the GMR for that serotype was greater than 0.5 (2-fold criterion).

Statistical analysis title	NI of Cohort 2 to Cohort 1 (60-64 yrs)

Statistical analysis description:

Serotype 23F: GMR (20vPnC Cohort 2 vs 20vPnC Cohort 1 60-64 years of age) and the 2-sided 95% CI

Comparison groups	Cohort 2: 20vPnC v Cohort 1: 20vPnC/Saline (60-64 Years of Age)
Number of subjects included in analysis	1267
Analysis specification	Pre-specified
Analysis type	non-inferiority[40]
Parameter estimate	Ratio of GMTs
Point estimate	1.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.27
upper limit	2.22

Notes:

[40] - Noninferiority for a serotype was declared if the lower bound of the 2-sided 95% CI for the GMR for that serotype was greater than 0.5 (2-fold criterion).

Statistical analysis title	NI of Cohort 2 to Cohort 1 (60-64 yrs)

Statistical analysis description:

Serotype 8: GMR (20vPnC Cohort 2 vs 20vPnC Cohort 1 60-64 years of age) and the 2-sided 95% CI

Comparison groups	Cohort 2: 20vPnC v Cohort 1: 20vPnC/Saline (60-64 Years of Age)

Number of subjects included in analysis	1267
Analysis specification	Pre-specified
Analysis type	non-inferiority[41]
Parameter estimate	Ratio of GMTs
Point estimate	0.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.78
upper limit	1.2

Notes:

[41] - Noninferiority for a serotype was declared if the lower bound of the 2-sided 95% CI for the GMR for that serotype was greater than 0.5 (2-fold criterion).

Statistical analysis title	NI of Cohort 2 to Cohort 1 (60-64 yrs)

Statistical analysis description:

Serotype 10A: GMR (20vPnC Cohort 2 vs 20vPnC Cohort 1 60-64 years of age) and the 2-sided 95% CI

Comparison groups	Cohort 2: 20vPnC v Cohort 1: 20vPnC/Saline (60-64 Years of Age)
Number of subjects included in analysis	1267
Analysis specification	Pre-specified
Analysis type	non-inferiority[42]
Parameter estimate	Ratio of GMTs
Point estimate	1.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.84
upper limit	1.28

Notes:

[42] - Noninferiority for a serotype was declared if the lower bound of the 2-sided 95% CI for the GMR for that serotype was greater than 0.5 (2-fold criterion).

Statistical analysis title	NI of Cohort 2 to Cohort 1 (60-64 yrs)

Statistical analysis description:

Serotype 11A: GMR (20vPnC Cohort 2 vs 20vPnC Cohort 1 60-64 years of age) and the 2-sided 95% CI

Comparison groups	Cohort 2: 20vPnC v Cohort 1: 20vPnC/Saline (60-64 Years of Age)
Number of subjects included in analysis	1267
Analysis specification	Pre-specified
Analysis type	non-inferiority[43]
Parameter estimate	Ratio of GMTs
Point estimate	1.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.96
upper limit	1.56

Notes:

[43] - Noninferiority for a serotype was declared if the lower bound of the 2-sided 95% CI for the GMR for that serotype was greater than 0.5 (2-fold criterion).

Statistical analysis title	NI of Cohort 2 to Cohort 1 (60-64 yrs)

Statistical analysis description:	
Serotype 12F: GMR (20vPnC Cohort 2 vs 20vPnC Cohort 1 60-64 years of age) and the 2-sided 95% CI	
Comparison groups	Cohort 2: 20vPnC v Cohort 1: 20vPnC/Saline (60-64 Years of Age)
Number of subjects included in analysis	1267
Analysis specification	Pre-specified
Analysis type	non-inferiority[44]
Parameter estimate	Ratio of GMTs
Point estimate	1.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.88
upper limit	1.39

Notes:

[44] - Noninferiority for a serotype was declared if the lower bound of the 2-sided 95% CI for the GMR for that serotype was greater than 0.5 (2-fold criterion).

Statistical analysis title	NI of Cohort 2 to Cohort 1 (60-64 yrs)
Statistical analysis description:	
Serotype 15B: GMR (20vPnC Cohort 2 vs 20vPnC Cohort 1 60-64 years of age) and the 2-sided 95% CI	
Comparison groups	Cohort 2: 20vPnC v Cohort 1: 20vPnC/Saline (60-64 Years of Age)
Number of subjects included in analysis	1267
Analysis specification	Pre-specified
Analysis type	non-inferiority[45]
Parameter estimate	Ratio of GMTs
Point estimate	1.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.88
upper limit	1.56

Notes:

[45] - Noninferiority for a serotype was declared if the lower bound of the 2-sided 95% CI for the GMR for that serotype was greater than 0.5 (2-fold criterion).

Statistical analysis title	NI of Cohort 2 to Cohort 1 (60-64 yrs)
Statistical analysis description:	
Serotype 22F: GMR (20vPnC Cohort 2 vs 20vPnC Cohort 1 60-64 years of age) and the 2-sided 95% CI	
Comparison groups	Cohort 2: 20vPnC v Cohort 1: 20vPnC/Saline (60-64 Years of Age)
Number of subjects included in analysis	1267
Analysis specification	Pre-specified
Analysis type	non-inferiority[46]
Parameter estimate	Ratio of GMTs
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.69
upper limit	1.17

Notes:

[46] - Noninferiority for a serotype was declared if the lower bound of the 2-sided 95% CI for the GMR for that serotype was greater than 0.5 (2-fold criterion).

Statistical analysis title	NI of Cohort 2 to Cohort 1 (60-64 yrs)
Statistical analysis description:	
Serotype 33F: GMR (20vPnC Cohort 2 vs 20vPnC Cohort 1 60-64 years of age) and the 2-sided 95% CI	
Comparison groups	Cohort 2: 20vPnC v Cohort 1: 20vPnC/Saline (60-64 Years of Age)
Number of subjects included in analysis	1267
Analysis specification	Pre-specified
Analysis type	non-inferiority[47]
Parameter estimate	Ratio of GMTs
Point estimate	1.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.81
upper limit	1.3

Notes:

[47] - Noninferiority for a serotype was declared if the lower bound of the 2-sided 95% CI for the GMR for that serotype was greater than 0.5 (2-fold criterion).

Secondary: Pneumococcal OPA GMTs for the 20 Vaccines Serotypes at 1 Month After 20vPnC Vaccination in Cohort 3, 18 Through 49 Years and Cohort 1, Only 60 Through 64 Years of Age: Evaluable-20 Immunogenicity Population

End point title	Pneumococcal OPA GMTs for the 20 Vaccines Serotypes at 1 Month After 20vPnC Vaccination in Cohort 3, 18 Through 49 Years and Cohort 1, Only 60 Through 64 Years of Age: Evaluable-20 Immunogenicity Population[48]

End point description:

OPA GMTs were determined for serotypes: 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F, 8, 10A, 11A, 12F, 15B, 22F and 33F. OPA titer was expressed as reciprocal of the highest serum dilution. OPA geometric mean and 2-sided 95% CIs were calculated. Evaluable-20 immunogenicity population included subjects who were enrolled in the appropriate cohort based on age, received the vaccination as randomized, had at least 1 valid OPA titer from the blood collection 27 to 49 days after 20vPnC, had no other major protocol deviations. Here, "n" =subjects evaluable for this endpoint at specified rows.

End point type	Secondary

End point timeframe:

1 month after vaccination

Notes:

[48] - 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 for reporting arms “Cohort 1: 20vPnC/Saline” and “Cohort 1: 13vPnC/PPSV23” only.

End point values	Cohort 3: 20vPnC	Cohort 1: 20vPnC/Saline (60-64 Years of Age)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	317	946		
Units: titer				
geometric mean (confidence interval 95%)				
Serotype 1 (n =316, 941)	162.6 (135.1 to 195.6)	132.0 (117.7 to 148.1)		

Serotype 3 (n =316, 935)	42.1 (36.9 to 48.1)	42.0 (38.7 to 45.7)		
Serotype 4 (n =315, 931)	1966.7 (1599.5 to 2418.3)	594.5 (522.9 to 675.9)		
Serotype 5 (n =317, 935)	107.9 (89.4 to 130.1)	96.9 (86.2 to 109.0)		
Serotype 6A (n =315, 921)	3930.5 (3176.0 to 4864.4)	1022.8 (896.1 to 1167.4)		
Serotype 6B (n =314, 933)	4260.0 (3461.3 to 5243.1)	1250.4 (1102.3 to 1418.4)		
Serotype 7F (n =311, 924)	1872.8 (1564.2 to 2242.4)	1187.2 (1064.4 to 1324.2)		
Serotype 9V (n =315, 922)	6041.4 (4962.5 to 7354.9)	1726.7 (1529.2 to 1949.7)		
Serotype 14 (n =316, 933)	1848.4 (1514.7 to 2255.7)	772.8 (684.7 to 872.3)		
Serotype 18C (n =312, 937)	4460.5 (3584.6 to 5550.4)	1395.3 (1220.9 to 1594.5)		
Serotype 19A (n =312, 932)	1415.0 (1181.8 to 1694.2)	611.3 (547.8 to 682.3)		
Serotype 19F (n =315, 937)	654.8 (538.2 to 796.8)	301.2 (266.7 to 340.1)		
Serotype 23F (n =315, 937)	1559.2 (1208.1 to 2012.2)	324.5 (277.1 to 380.1)		
Serotype 8 (n =306, 901)	867.0 (709.7 to 1059.2)	508.1 (448.8 to 575.3)		
Serotype 10A (n =292, 857)	4157.3 (3410.9 to 5067.0)	2569.7 (2274.0 to 2903.7)		
Serotype 11A (n =263, 796)	7169.3 (5735.7 to 8961.1)	5419.7 (4737.7 to 6199.7)		
Serotype 12F (n =273, 855)	5875.4 (4719.8 to 7314.1)	3074.5 (2697.9 to 3503.7)		
Serotype 15B (n =279, 830)	4601.0 (3487.9 to 6069.4)	3019.0 (2562.8 to 3556.4)		
Serotype 22F (n =273, 835)	7568.2 (5927.4 to 9663.2)	4482.5 (3862.7 to 5201.8)		
Serotype 33F (n =251, 765)	7976.9 (6341.7 to 10033.7)	5693.2 (4970.1 to 6521.5)		

Statistical analyses

Statistical analysis title	NI of Cohort 3 to Cohort 1 (60-64 yrs)
Statistical analysis description:	
Serotype 1: GMR (20vPnC Cohort 3 vs 20vPnC Cohort 1 60-64 years of age) and the 2-sided 95% CI	
Comparison groups	Cohort 3: 20vPnC v Cohort 1: 20vPnC/Saline (60-64 Years of

	Age)
Number of subjects included in analysis	1263
Analysis specification	Pre-specified
Analysis type	non-inferiority[49]
Parameter estimate	Ratio of GMTs
Point estimate	1.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.01
upper limit	1.5

Notes:

[49] - Noninferiority for a serotype was declared if the lower bound of the 2-sided 95% CI for the GMR for that serotype was greater than 0.5 (2-fold criterion).

Statistical analysis title	NI of Cohort 3 to Cohort 1 (60-64 yrs)

Statistical analysis description:

Serotype 3: GMR (20vPnC Cohort 3 vs 20vPnC Cohort 1 60-64 years of age) and the 2-sided 95% CI

Comparison groups	Cohort 3: 20vPnC v Cohort 1: 20vPnC/Saline (60-64 Years of Age)
Number of subjects included in analysis	1263
Analysis specification	Pre-specified
Analysis type	non-inferiority[50]
Parameter estimate	Ratio of GMTs
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.87
upper limit	1.16

Notes:

[50] - Noninferiority for a serotype was declared if the lower bound of the 2-sided 95% CI for the GMR for that serotype was greater than 0.5 (2-fold criterion).

Statistical analysis title	NI of Cohort 3 to Cohort 1 (60-64 yrs)

Statistical analysis description:

Serotype 4: GMR (20vPnC Cohort 3 vs 20vPnC Cohort 1 60-64 years of age) and the 2-sided 95% CI

Comparison groups	Cohort 3: 20vPnC v Cohort 1: 20vPnC/Saline (60-64 Years of Age)
Number of subjects included in analysis	1263
Analysis specification	Pre-specified
Analysis type	non-inferiority[51]
Parameter estimate	Ratio of GMTs
Point estimate	3.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.65
upper limit	4.13

Notes:

[51] - Noninferiority for a serotype was declared if the lower bound of the 2-sided 95% CI for the GMR for that serotype was greater than 0.5 (2-fold criterion).

Statistical analysis title	NI of Cohort 3 to Cohort 1 (60-64 yrs)
Statistical analysis description:	
Serotype 5: GMR (20vPnC Cohort 3 vs 20vPnC Cohort 1 60-64 years of age) and the 2-sided 95% CI	
Comparison groups	Cohort 3: 20vPnC v Cohort 1: 20vPnC/Saline (60-64 Years of Age)
Number of subjects included in analysis	1263
Analysis specification	Pre-specified
Analysis type	non-inferiority[52]
Parameter estimate	Ratio of GMTs
Point estimate	1.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.91
upper limit	1.36

Notes:

[52] - Noninferiority for a serotype was declared if the lower bound of the 2-sided 95% CI for the GMR for that serotype was greater than 0.5 (2-fold criterion).

Statistical analysis title	NI of Cohort 3 to Cohort 1 (60-64 yrs)
Statistical analysis description:	
Serotype 6A: GMR (20vPnC Cohort 3 vs 20vPnC Cohort 1 60-64 years of age) and the 2-sided 95% CI	
Comparison groups	Cohort 3: 20vPnC v Cohort 1: 20vPnC/Saline (60-64 Years of Age)
Number of subjects included in analysis	1263
Analysis specification	Pre-specified
Analysis type	non-inferiority[53]
Parameter estimate	Ratio of GMTs
Point estimate	3.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.06
upper limit	4.83

Notes:

[53] - Noninferiority for a serotype was declared if the lower bound of the 2-sided 95% CI for the GMR for that serotype was greater than 0.5 (2-fold criterion).

Statistical analysis title	NI of Cohort 3 to Cohort 1 (60-64 yrs)
Statistical analysis description:	
Serotype 6B: GMR (20vPnC Cohort 3 vs 20vPnC Cohort 1 60-64 years of age) and the 2-sided 95% CI	
Comparison groups	Cohort 3: 20vPnC v Cohort 1: 20vPnC/Saline (60-64 Years of Age)
Number of subjects included in analysis	1263
Analysis specification	Pre-specified
Analysis type	non-inferiority[54]
Parameter estimate	Ratio of GMTs
Point estimate	3.41
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.73
upper limit	4.26

Notes:

[54] - Noninferiority for a serotype was declared if the lower bound of the 2-sided 95% CI for the GMR for that serotype was greater than 0.5 (2-fold criterion).

Statistical analysis title	NI of Cohort 3 to Cohort 1 (60-64 yrs)
Statistical analysis description:	
Serotype 7F: GMR (20vPnC Cohort 3 vs 20vPnC Cohort 1 60-64 years of age) and the 2-sided 95% CI	
Comparison groups	Cohort 3: 20vPnC v Cohort 1: 20vPnC/Saline (60-64 Years of Age)
Number of subjects included in analysis	1263
Analysis specification	Pre-specified
Analysis type	non-inferiority[55]
Parameter estimate	Ratio of GMTs
Point estimate	1.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.3
upper limit	1.91

Notes:

[55] - Noninferiority for a serotype was declared if the lower bound of the 2-sided 95% CI for the GMR for that serotype was greater than 0.5 (2-fold criterion).

Statistical analysis title	NI of Cohort 3 to Cohort 1 (60-64 yrs)
Statistical analysis description:	
Serotype 9V: GMR (20vPnC Cohort 3 vs 20vPnC Cohort 1 60-64 years of age) and the 2-sided 95% CI	
Comparison groups	Cohort 3: 20vPnC v Cohort 1: 20vPnC/Saline (60-64 Years of Age)
Number of subjects included in analysis	1263
Analysis specification	Pre-specified
Analysis type	non-inferiority[56]
Parameter estimate	Ratio of GMTs
Point estimate	3.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.83
upper limit	4.33

Notes:

[56] - Noninferiority for a serotype was declared if the lower bound of the 2-sided 95% CI for the GMR for that serotype was greater than 0.5 (2-fold criterion).

Statistical analysis title	NI of Cohort 3 to Cohort 1 (60-64 yrs)
Statistical analysis description:	
Serotype 14: GMR (20vPnC Cohort 3 vs 20vPnC Cohort 1 60-64 years of age) and the 2-sided 95% CI	
Comparison groups	Cohort 3: 20vPnC v Cohort 1: 20vPnC/Saline (60-64 Years of Age)
Number of subjects included in analysis	1263
Analysis specification	Pre-specified
Analysis type	non-inferiority[57]
Parameter estimate	Ratio of GMTs
Point estimate	2.39

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.93
upper limit	2.96

Notes:

[57] - Noninferiority for a serotype was declared if the lower bound of the 2-sided 95% CI for the GMR for that serotype was greater than 0.5 (2-fold criterion).

Statistical analysis title	NI of Cohort 3 to Cohort 1 (60-64 yrs)

Statistical analysis description:

Serotype 18C: GMR (20vPnC Cohort 3 vs 20vPnC Cohort 1 60-64 years of age) and the 2-sided 95% CI

Comparison groups	Cohort 3: 20vPnC v Cohort 1: 20vPnC/Saline (60-64 Years of Age)
Number of subjects included in analysis	1263
Analysis specification	Pre-specified
Analysis type	non-inferiority[58]
Parameter estimate	Ratio of GMTs
Point estimate	3.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.53
upper limit	4.04

Notes:

[58] - Noninferiority for a serotype was declared if the lower bound of the 2-sided 95% CI for the GMR for that serotype was greater than 0.5 (2-fold criterion).

Statistical analysis title	NI of Cohort 3 to Cohort 1 (60-64 yrs)

Statistical analysis description:

Serotype 19A: GMR (20vPnC Cohort 3 vs 20vPnC Cohort 1 60-64 years of age) and the 2-sided 95% CI

Comparison groups	Cohort 3: 20vPnC v Cohort 1: 20vPnC/Saline (60-64 Years of Age)
Number of subjects included in analysis	1263
Analysis specification	Pre-specified
Analysis type	non-inferiority[59]
Parameter estimate	Ratio of GMTs
Point estimate	2.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.91
upper limit	2.81

Notes:

[59] - Noninferiority for a serotype was declared if the lower bound of the 2-sided 95% CI for the GMR for that serotype was greater than 0.5 (2-fold criterion).

Statistical analysis title	NI of Cohort 3 to Cohort 1 (60-64 yrs)

Statistical analysis description:

Serotype 19F: GMR (20vPnC Cohort 3 vs 20vPnC Cohort 1 60-64 years of age) and the 2-sided 95% CI

Comparison groups	Cohort 3: 20vPnC v Cohort 1: 20vPnC/Saline (60-64 Years of Age)

Number of subjects included in analysis	1263
Analysis specification	Pre-specified
Analysis type	non-inferiority[60]
Parameter estimate	Ratio of GMTs
Point estimate	2.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.76
upper limit	2.68

Notes:

[60] - Noninferiority for a serotype was declared if the lower bound of the 2-sided 95% CI for the GMR for that serotype was greater than 0.5 (2-fold criterion).

Statistical analysis title	NI of Cohort 3 to Cohort 1 (60-64 yrs)

Statistical analysis description:

Serotype 23F: GMR (20vPnC Cohort 3 vs 20vPnC Cohort 1 60-64 years of age) and the 2-sided 95% CI

Comparison groups	Cohort 3: 20vPnC v Cohort 1: 20vPnC/Saline (60-64 Years of Age)
Number of subjects included in analysis	1263
Analysis specification	Pre-specified
Analysis type	non-inferiority[61]
Parameter estimate	Ratio of GMTs
Point estimate	4.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.65
upper limit	6.32

Notes:

[61] - Noninferiority for a serotype was declared if the lower bound of the 2-sided 95% CI for the GMR for that serotype was greater than 0.5 (2-fold criterion).

Statistical analysis title	NI of Cohort 3 to Cohort 1 (60-64 yrs)

Statistical analysis description:

Serotype 8: GMR (20vPnC Cohort 3 vs 20vPnC Cohort 1 60-64 years of age) and the 2-sided 95% CI

Comparison groups	Cohort 3: 20vPnC v Cohort 1: 20vPnC/Saline (60-64 Years of Age)
Number of subjects included in analysis	1263
Analysis specification	Pre-specified
Analysis type	non-inferiority[62]
Parameter estimate	Ratio of GMTs
Point estimate	1.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.38
upper limit	2.12

Notes:

[62] - Noninferiority for a serotype was declared if the lower bound of the 2-sided 95% CI for the GMR for that serotype was greater than 0.5 (2-fold criterion).

Statistical analysis title	NI of Cohort 3 to Cohort 1 (60-64 yrs)

Statistical analysis description:

Serotype 10A: GMR (20vPnC Cohort 3 vs 20vPnC Cohort 1 60-64 years of age) and the 2-sided 95% CI

Comparison groups	Cohort 3: 20vPnC v Cohort 1: 20vPnC/Saline (60-64 Years of Age)
Number of subjects included in analysis	1263
Analysis specification	Pre-specified
Analysis type	non-inferiority[63]
Parameter estimate	Ratio of GMTs
Point estimate	1.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.31
upper limit	2

Notes:

[63] - Noninferiority for a serotype was declared if the lower bound of the 2-sided 95% CI for the GMR for that serotype was greater than 0.5 (2-fold criterion).

Statistical analysis title	NI of Cohort 3 to Cohort 1 (60-64 yrs)

Statistical analysis description:

Serotype 11A: GMR (20vPnC Cohort 3 vs 20vPnC Cohort 1 60-64 years of age) and the 2-sided 95% CI

Comparison groups	Cohort 3: 20vPnC v Cohort 1: 20vPnC/Saline (60-64 Years of Age)
Number of subjects included in analysis	1263
Analysis specification	Pre-specified
Analysis type	non-inferiority[64]
Parameter estimate	Ratio of GMTs
Point estimate	1.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.04
upper limit	1.68

Notes:

[64] - Noninferiority for a serotype was declared if the lower bound of the 2-sided 95% CI for the GMR for that serotype was greater than 0.5 (2-fold criterion).

Statistical analysis title	NI of Cohort 3 to Cohort 1 (60-64 yrs)

Statistical analysis description:

Serotype 12F: GMR (20vPnC Cohort 3 vs 20vPnC Cohort 1 60-64 years of age) and the 2-sided 95% CI

Comparison groups	Cohort 3: 20vPnC v Cohort 1: 20vPnC/Saline (60-64 Years of Age)
Number of subjects included in analysis	1263
Analysis specification	Pre-specified
Analysis type	non-inferiority[65]
Parameter estimate	Ratio of GMTs
Point estimate	1.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.51
upper limit	2.41

Notes:

[65] - Noninferiority for a serotype was declared if the lower bound of the 2-sided 95% CI for the GMR for that serotype was greater than 0.5 (2-fold criterion).

Statistical analysis title	NI of Cohort 3 to Cohort 1 (60-64 yrs)
Statistical analysis description:	
Serotype 15B: GMR (20vPnC Cohort 3 vs 20vPnC Cohort 1 60-64 years of age) and the 2-sided 95% CI	
Comparison groups	Cohort 3: 20vPnC v Cohort 1: 20vPnC/Saline (60-64 Years of Age)
Number of subjects included in analysis	1263
Analysis specification	Pre-specified
Analysis type	non-inferiority[66]
Parameter estimate	Ratio of GMTs
Point estimate	1.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.13
upper limit	2.05

Notes:

[66] - Noninferiority for a serotype was declared if the lower bound of the 2-sided 95% CI for the GMR for that serotype was greater than 0.5 (2-fold criterion).

Statistical analysis title	NI of Cohort 3 to Cohort 1 (60-64 yrs)
Statistical analysis description:	
Serotype 22F: GMR (20vPnC Cohort 3 vs 20vPnC Cohort 1 60-64 years of age) and the 2-sided 95% CI	
Comparison groups	Cohort 3: 20vPnC v Cohort 1: 20vPnC/Saline (60-64 Years of Age)
Number of subjects included in analysis	1263
Analysis specification	Pre-specified
Analysis type	non-inferiority[67]
Parameter estimate	Ratio of GMTs
Point estimate	1.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.3
upper limit	2.2

Notes:

[67] - Noninferiority for a serotype was declared if the lower bound of the 2-sided 95% CI for the GMR for that serotype was greater than 0.5 (2-fold criterion).

Statistical analysis title	NI of Cohort 3 to Cohort 1 (60-64 yrs)
Statistical analysis description:	
Serotype 33F: GMR (20vPnC Cohort 3 vs 20vPnC Cohort 1 60-64 years of age) and the 2-sided 95% CI	
Comparison groups	Cohort 3: 20vPnC v Cohort 1: 20vPnC/Saline (60-64 Years of Age)
Number of subjects included in analysis	1263
Analysis specification	Pre-specified
Analysis type	non-inferiority[68]
Parameter estimate	Ratio of GMTs
Point estimate	1.4

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.1
upper limit	1.79

Notes:

[68] - Noninferiority for a serotype was declared if the lower bound of the 2-sided 95% CI for the GMR for that serotype was greater than 0.5 (2-fold criterion).

Secondary: Pneumococcal OPA Geometric Mean Fold Rises (GMFRs) for the 13 Matched Serotypes From Before Vaccination 1 to 1 Month After Vaccination 1 (20vPnC or 13vPnC) in Cohort 1: Evaluable 13-Matched Immunogenicity Population

End point title	Pneumococcal OPA Geometric Mean Fold Rises (GMFRs) for the 13 Matched Serotypes From Before Vaccination 1 to 1 Month After Vaccination 1 (20vPnC or 13vPnC) in Cohort 1: Evaluable 13-Matched Immunogenicity Population[69]

End point description:

OPA GMFR is the ratio of OPA GMT, 1 month after vaccination to before vaccination OPA GMT. OPA GMFRs from before to 1 month after vaccination 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. Evaluable 13-matched immunogenicity population included subjects who were enrolled in the appropriate cohort based on age, received Vaccination 1 as randomized, had at least 1 valid OPA titer for any of the 13 matched serotypes from the blood collection 27 to 49 days after Vaccination 1, had no other major protocol deviations. Here, "n" =subjects evaluable with OPA titers available at both timepoints at the specified row.

End point type	Secondary

End point timeframe:

Before Vaccination 1 to 1 month after Vaccination 1

Notes:

[69] - 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 for reporting arms “Cohort 1: 20vPnC/Saline” and “Cohort 1: 13vPnC/PPSV23” only.

End point values	Cohort 1: 20vPnC/Saline	Cohort 1: 13vPnC/PPSV23		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1435	1420		
Units: fold rise				
geometric mean (confidence interval 95%)				
Serotype 1 (n =1425, 1418)	12.6 (11.5 to 13.8)	15.4 (14.1 to 16.8)		
Serotype 3 (n =1404, 1401)	4.8 (4.5 to 5.2)	5.8 (5.4 to 6.2)		
Serotype 4 (n =1370, 1374)	31.2 (27.8 to 34.9)	39.3 (35.1 to 44.1)		
Serotype 5 (n =1411, 1394)	6.1 (5.6 to 6.6)	7.2 (6.6 to 7.8)		
Serotype 6A (n =1382,1371)	34.3 (30.7 to 38.3)	42.6 (38.2 to 47.5)		
Serotype 6B (n =1360, 1360)	23.8 (21.3 to 26.6)	26.5 (23.7 to 29.6)		
Serotype 7F (n =1367, 1355)	12.2 (11.1 to 13.3)	13.5 (12.3 to 14.8)		
Serotype 9V (n =1317, 1294)	11.0 (9.9 to 12.2)	12.5 (11.3 to 13.9)		
Serotype 14 (n =1370, 1366)	9.3 (8.3 to 10.3)	8.3 (7.4 to 9.2)		

Serotype 18C (n =1407, 1396)	33.8 (30.0 to 38.1)	37.7 (33.5 to 42.5)		
Serotype 19A (n =1400, 1379)	21.0 (19.0 to 23.3)	25.9 (23.3 to 28.8)		
Serotype 19F (n =1405, 1397)	8.6 (7.9 to 9.5)	10.8 (9.8 to 11.9)		
Serotype 23F (n =1409, 1402)	24.9 (22.0 to 28.1)	30.7 (27.1 to 34.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pneumococcal OPA GMFRs for the Additional 7 Serotypes From Before Vaccination 1 to 1 Month After Vaccination 1 (20vPnC) or From Before Vaccination 1 to 1 Month After Vaccination 2 (PPSV23) in Cohort 1: Evaluable 7-Additional Immunogenicity Population

End point title	Pneumococcal OPA GMFRs for the Additional 7 Serotypes From Before Vaccination 1 to 1 Month After Vaccination 1 (20vPnC) or From Before Vaccination 1 to 1 Month After Vaccination 2 (PPSV23) in Cohort 1: Evaluable 7-Additional Immunogenicity Population[70]

End point description:

OPA GMFR is the ratio of OPA GMT, 1 month after vaccination to before vaccination OPA GMT. OPA GMFRs from before to 1 month after vaccination were calculated along with corresponding 2-sided 95% CIs for pneumococcal serotypes 8, 10A, 11A, 12F, 15B, 22F and 33F. Evaluable 7-additional immunogenicity population included subjects who were enrolled in appropriate cohort based on age, received 20vPnC if randomized to 20vPnC/saline group or received both vaccinations if randomized to 13vPnC/PPSV23 group, had at least 1 valid OPA titers for any of 7 additional serotypes from blood collection 27 to 49 days after Vaccination 1 or Vaccination 2 respectively, had no other major protocol deviations. Here, "n" =subjects evaluable with OPA titers available at both timepoints at specified row.

End point type	Secondary

End point timeframe:

From before Vaccination 1 to 1 month after Vaccination 1 in "Cohort 1: 20vPnC/Saline" or From before Vaccination 1 to 1 month after Vaccination 2 in "Cohort 1: 13vPnC/PPSV23"

Notes:

[70] - 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 for reporting arms "Cohort 1: 20vPnC/Saline" and "Cohort 1: 13vPnC/PPSV23" only.

End point values	Cohort 1: 20vPnC/Saline	Cohort 1: 13vPnC/PPSV23		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1433	1383		
Units: fold rise				
geometric mean (confidence interval 95%)				
Serotype 8 (n =1353, 1293)	22.1 (20.0 to 24.5)	40.4 (36.6 to 44.7)		
Serotype 10A (n =1208, 1164)	18.5 (16.5 to 20.6)	10.1 (9.1 to 11.3)		
Serotype 11A (n =973, 993)	9.3 (8.1 to 10.7)	6.0 (5.3 to 6.9)		
Serotype 12F (n =1226, 1147)	72.4 (64.2 to 81.6)	47.3 (41.4 to 54.1)		

Serotype 15B (n =1228, 1178)	55.4 (47.7 to 64.4)	18.2 (15.6 to 21.1)		
Serotype 22F (n =1178, 1156)	78.5 (67.3 to 91.5)	37.9 (32.7 to 43.9)		
Serotype 33F (n =1020, 1080)	7.5 (6.7 to 8.5)	5.7 (5.1 to 6.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pneumococcal OPA GMFRs for the 20 Vaccines Serotypes From Before Vaccination to 1 Month After Vaccination in Cohort 2 and 3: Evaluable-20 Immunogenicity Population

End point title	Pneumococcal OPA GMFRs for the 20 Vaccines Serotypes From Before Vaccination to 1 Month After Vaccination in Cohort 2 and 3: Evaluable-20 Immunogenicity Population[71]

End point description:

OPA GMFR is the ratio of OPA GMT, 1 month after vaccination to before vaccination OPA GMT. OPA GMFRs from before to 1 month after vaccination were calculated along with corresponding 2-sided 95% CIs for pneumococcal serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F, 8, 10A, 11A, 12F, 15B, 22F and 33F. Evaluable-20 immunogenicity population included subjects who were enrolled in the appropriate cohort based on age, received the vaccination as randomized, had at least 1 valid OPA titer from the blood collection 27 to 49 days after 20vPnC, had no other major protocol deviations. Here, "n" =subjects evaluable with OPA titers available at both timepoints at the specified row.

End point type	Secondary

End point timeframe:

Before vaccination to 1 month after vaccination

Notes:

[71] - 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 for reporting arms “Cohort 1: 20vPnC/Saline” and “Cohort 1: 13vPnC/PPSV23” only.

End point values	Cohort 2: 20vPnC	Cohort 3: 20vPnC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	321	317		
Units: Fold rise				
geometric mean (confidence interval 95%)				
Serotype 1 (n =319, 315)	14.4 (12.0 to 17.3)	18.6 (16.0 to 21.8)		
Serotype 3 (n =317, 312)	5.1 (4.4 to 5.9)	4.8 (4.2 to 5.5)		
Serotype 4 (n =304, 302)	43.4 (34.4 to 54.9)	131.8 (106.4 to 163.4)		
Serotype 5 (n =312,315)	5.9 (5.0 to 7.0)	7.9 (6.7 to 9.4)		
Serotype 6A (n =312, 305)	50.3 (40.2 to 63.0)	146.5 (120.6 to 178.0)		
Serotype 6B (n =299, 286)	31.7 (25.3 to 39.7)	70.3 (55.7 to 88.7)		
Serotype 7F (n =300, 284)	12.8 (10.7 to 15.4)	19.7 (16.1 to 24.3)		
Serotype 9V (n =288, 281)	12.1 (9.9 to 14.7)	35.1 (27.9 to 44.2)		

Serotype 14 (n =300, 291)	10.4 (8.3 to 13.0)	14.6 (11.3 to 18.9)		
Serotype 18C (n =308, 299)	48.3 (37.9 to 61.5)	111.8 (86.8 to 143.8)		
Serotype 19A (n =310, 299)	23.6 (19.2 to 29.1)	39.1 (30.9 to 49.6)		
Serotype 19F (n =316, 310)	9.2 (7.6 to 11.3)	17.8 (14.7 to 21.6)		
Serotype 23F (n =313, 309)	47.8 (37.2 to 61.3)	118.2 (92.7 to 150.7)		
Serotype 8 (n =310, 300)	23.9 (19.3 to 29.6)	34.6 (27.8 to 43.0)		
Serotype 10A (n =273, 260)	17.9 (14.2 to 22.6)	22.7 (17.8 to 29.0)		
Serotype 11A (n =213, 220)	10.4 (7.7 to 14.2)	5.2 (3.9 to 6.9)		
Serotype 12F (n =279, 252)	107.3 (85.8 to 134.1)	171.1 (135.1 to 216.8)		
Serotype 15B (n =263, 248)	72.1 (51.9 to 100.1)	65.0 (44.8 to 94.4)		
Serotype 22F (n =256, 241)	63.5 (44.8 to 90.1)	69.3 (48.4 to 99.4)		
Serotype 33F (n =233, 213)	9.1 (7.1 to 11.7)	7.5 (5.8 to 9.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With >=4-Fold Rise in Pneumococcal OPA Titers to the 13 Matched Serotypes From Before Vaccination 1 to 1 Month After Vaccination 1 (20vPnC or 13vPnC) in Cohort 1: Evaluable 13-Matched Immunogenicity Population

End point title	Percentage of Subjects With >=4-Fold Rise in Pneumococcal OPA Titers to the 13 Matched Serotypes From Before Vaccination 1 to 1 Month After Vaccination 1 (20vPnC or 13vPnC) in Cohort 1: Evaluable 13-Matched Immunogenicity Population[72]

End point description:

Percentage of subjects with a >=4-fold rise in serotype-specific pneumococcal OPA titers from before vaccination to 1 month after vaccination along with corresponding 2-sided 95% CIs were calculated for pneumococcal serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F and 23F. Evaluable 13-matched immunogenicity population included subjects who were enrolled in the appropriate cohort based on age, received Vaccination 1 as randomized, had at least 1 valid OPA titer for any of the 13 matched serotypes from the blood collection 27 to 49 days after Vaccination 1, had no other major protocol deviations. Here, "n" =subjects evaluable for this endpoint at specified rows.

End point type	Secondary

End point timeframe:

Before Vaccination 1 to 1 month after Vaccination 1

Notes:

[72] - 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 for reporting arms “Cohort 1: 20vPnC/Saline” and “Cohort 1: 13vPnC/PPSV23” only.

End point values	Cohort 1: 20vPnC/Saline	Cohort 1: 13vPnC/PPSV23		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1435	1420		
Units: percentage of subjects				
number (confidence interval 95%)				
Serotype 1 (n =1425, 1418)	72.1 (69.7 to 74.4)	74.8 (72.4 to 77.0)		
Serotype 3 (n =1404, 1401)	56.1 (53.4 to 58.7)	61.7 (59.1 to 64.2)		
Serotype 4 (n =1370, 1374)	75.5 (73.2 to 77.8)	79.6 (77.4 to 81.7)		
Serotype 5 (n =1411, 1394)	55.6 (52.9 to 58.2)	60.6 (58.0 to 63.2)		
Serotype 6A (n =1382, 1371)	80.5 (78.3 to 82.5)	84.0 (82.0 to 85.9)		
Serotype 6B (n =1360, 1360)	75.7 (73.3 to 77.9)	77.6 (75.3 to 79.8)		
Serotype 7F (n =1367, 1355)	71.8 (69.3 to 74.1)	72.3 (69.8 to 74.6)		
Serotype 9V (n =1317, 1294)	67.7 (65.1 to 70.3)	69.3 (66.7 to 71.8)		
Serotype 14 (n =1370, 1366)	58.2 (55.5 to 60.8)	54.0 (51.3 to 56.6)		
Serotype 18C (n =1407, 1396)	77.7 (75.4 to 79.8)	79.6 (77.4 to 81.7)		
Serotype 19A (n =1400, 1379)	73.6 (71.3 to 75.9)	77.5 (75.2 to 79.7)		
Serotype 19F (n =1405, 1397)	63.6 (61.1 to 66.2)	66.9 (64.4 to 69.4)		
Serotype 23F (n =1409, 1402)	70.6 (68.2 to 73.0)	74.4 (72.0 to 76.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With >=4-Fold Rise in Pneumococcal OPA Titers for the 7 Additional Serotypes From Before Vaccination 1 to 1 Month After Vaccination 1(20vPnC) or From Before Vaccination 1 to 1 Month After Vaccination 2(PPSV23) in Cohort 1:E7-AIP

End point title	Percentage of Subjects With >=4-Fold Rise in Pneumococcal OPA Titers for the 7 Additional Serotypes From Before Vaccination 1 to 1 Month After Vaccination 1(20vPnC) or From Before Vaccination 1 to 1 Month After Vaccination 2(PPSV23) in Cohort 1:E7-AIP[73]

End point description:

Percentage of subjects with a >=4-fold rise in serotype-specific pneumococcal OPA titers from before vaccination to 1 month after vaccination along with corresponding 2-sided 95% CIs were calculated for pneumococcal serotypes 8, 10A, 11A, 12F, 15B, 22F and 33F. E7-AIP included subjects who were enrolled in appropriate cohort based on age, received 20vPnC if randomized to 20vPnC/saline group or received both vaccinations if randomized to 13vPnC/PPSV23 group, had at least 1 valid OPA titers for any of 7 additional serotypes from blood collection 27 to 49 days after Vaccination 1 or Vaccination 2 respectively, had no other major protocol deviations. Here, "n" =subjects evaluable for this endpoint at specified rows.

End point type	Secondary

End point timeframe:

Before Vaccination 1 to 1 month after Vaccination 1 for "Cohort 1: 20vPnC/Saline"; Before Vaccination 1 to 1 month after Vaccination 2 for "Cohort 1: 13vPnC/PPSV23"

Notes:

[73] - 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 for reporting arms "Cohort 1: 20vPnC/Saline" and "Cohort 1: 13vPnC/PPSV23" only.

End point values	Cohort 1: 20vPnC/Saline	Cohort 1: 13vPnC/PPSV23		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1433	1383		
Units: percentage of subjects				
number (confidence interval 95%)				
Serotype 8 (n =1353, 1293)	77.8 (75.5 to 80.0)	86.8 (84.8 to 88.6)		
Serotype 10A (n =1208, 1164)	75.5 (73.0 to 77.9)	65.6 (62.8 to 68.4)		
Serotype 11A (n =973, 993)	59.2 (56.0 to 62.3)	51.9 (48.7 to 55.0)		
Serotype 12F (n =1226, 1147)	87.4 (85.5 to 89.2)	80.6 (78.1 to 82.8)		
Serotype 15B (n =1228, 1178)	77.8 (75.3 to 80.1)	63.8 (61.0 to 66.6)		
Serotype 22F (n =1178, 1156)	82.7 (80.4 to 84.8)	76.8 (74.3 to 79.2)		
Serotype 33F (n =1020, 1080)	60.1 (57.0 to 63.1)	55.5 (52.4 to 58.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With >=4-Fold Rise in Pneumococcal OPA Titers for the 20 Vaccines Serotypes From Before Vaccination to 1 Month After Vaccination in Cohort 2 and 3: Evaluable-20 Immunogenicity Population

End point title	Percentage of Subjects With >=4-Fold Rise in Pneumococcal OPA Titers for the 20 Vaccines Serotypes From Before Vaccination to 1 Month After Vaccination in Cohort 2 and 3: Evaluable-20 Immunogenicity Population[74]

End point description:

Percentage of subjects with a >=4-fold rise in serotype-specific pneumococcal OPA titers from before vaccination to 1 month after vaccination along with corresponding 2-sided 95% CIs were calculated for pneumococcal serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F, 8, 10A, 11A, 12F, 15B, 22F and 33F. Evaluable-20 immunogenicity population included subjects who were enrolled in the appropriate cohort based on age, received the vaccination as randomized, had at least 1 valid OPA titer from the blood collection 27 to 49 days after 20vPnC, had no other major protocol deviations. Here, "n" =subjects evaluable for this endpoint at specified rows.

End point type	Secondary

End point timeframe:

Before vaccination to 1 month after vaccination

Notes:

[74] - 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 for reporting arms "Cohort 1: 20vPnC/Saline" and "Cohort 1: 13vPnC/PPSV23" only.

End point values	Cohort 2: 20vPnC	Cohort 3: 20vPnC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	321	317		
Units: Percentage of subjects				
number (confidence interval 95%)				
Serotype 1 (n =319, 315)	74.9 (69.8 to 79.6)	86.0 (81.7 to 89.7)		
Serotype 3 (n =317,312)	59.0 (53.4 to 64.5)	56.7 (51.0 to 62.3)		
Serotype 4 (n =304,302)	84.2 (79.6 to 88.1)	91.4 (87.6 to 94.3)		
Serotype 5 (n =312, 315)	54.8 (49.1 to 60.4)	64.8 (59.2 to 70.0)		
Serotype 6A (n =312, 305)	85.9 (81.5 to 89.6)	96.7 (94.1 to 98.4)		
Serotype 6B (n =299, 286)	78.9 (73.9 to 83.4)	89.2 (85.0 to 92.5)		
Serotype 7F (n =300, 284)	73.0 (67.6 to 77.9)	76.1 (70.7 to 80.9)		
Serotype 9V (n =288, 281)	73.6 (68.1 to 78.6)	84.0 (79.2 to 88.1)		
Serotype 14 (n =300, 291)	62.3 (56.6 to 67.8)	62.2 (56.4 to 67.8)		
Serotype 18C (n =308, 299)	82.5 (77.8 to 86.5)	87.3 (83.0 to 90.8)		
Serotype 19A (n =310, 299)	80.0 (75.1 to 84.3)	82.6 (77.8 to 86.7)		
Serotype 19F (n =316, 310)	64.2 (58.7 to 69.5)	78.4 (73.4 to 82.8)		
Serotype 23F (n =313, 309)	81.2 (76.4 to 85.3)	87.7 (83.5 to 91.1)		
Serotype 8 (n =310, 300)	79.4 (74.4 to 83.7)	83.0 (78.3 to 87.1)		
Serotype 10A (n =273, 260)	78.8 (73.4 to 83.5)	78.8 (73.4 to 83.6)		
Serotype 11A (n =213, 220)	61.0 (54.1 to 67.6)	47.3 (40.5 to 54.1)		
Serotype 12F (n =279, 252)	93.2 (89.6 to 95.9)	93.7 (89.9 to 96.3)		
Serotype 15B (n =263, 248)	82.5 (77.4 to 86.9)	73.4 (67.4 to 78.8)		
Serotype 22 F (n =256, 241)	80.5 (75.1 to 85.1)	83.8 (78.5 to 88.2)		
Serotype 33F (n =233, 213)	63.9 (57.4 to 70.1)	60.6 (53.7 to 67.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Pneumococcal OPA Titers >= Lower Limit of Quantitation (LLOQ) for the 13 Matched Serotypes at 1 Month After Vaccination 1 (20vPnC or 13vPnC) in Cohort 1: Evaluable 13-Matched Immunogenicity Population

End point title	Percentage of Subjects With Pneumococcal OPA Titers >= Lower Limit of Quantitation (LLOQ) for the 13 Matched Serotypes at 1 Month After Vaccination 1 (20vPnC or 13vPnC) in Cohort 1: Evaluable 13-Matched Immunogenicity Population[75]

End point description:

The percentage of subjects with OPA titers >=LLOQ along with corresponding 2-sided 95% CIs were calculated 1 month after vaccination for pneumococcal serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F and 23F. Evaluable 13-matched immunogenicity population included subjects who were enrolled in the appropriate cohort based on age, received Vaccination 1 as randomized, had at least 1 valid OPA titer for any of the 13 matched serotypes from the blood collection 27 to 49 days after Vaccination 1, had no other major protocol deviations. Here, "n" =subjects evaluable for this endpoint at specified rows.

End point type	Secondary

End point timeframe:

1 month after Vaccination 1

Notes:

[75] - 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 for reporting arms “Cohort 1: 20vPnC/Saline” and “Cohort 1: 13vPnC/PPSV23” only.

End point values	Cohort 1: 20vPnC/Saline	Cohort 1: 13vPnC/PPSV23		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1435	1420		
Units: Percentage of subjects				
number (confidence interval 95%)				
Serotype 1 (n =1430, 1419)	85.0 (83.0 to 86.8)	87.9 (86.1 to 89.5)		
Serotype 3 (n =1415, 1411)	84.2 (82.2 to 86.0)	87.0 (85.2 to 88.7)		
Serotype 4 (n =1415, 1409)	91.1 (89.5 to 92.5)	92.1 (90.5 to 93.4)		
Serotype 5 (n =1418, 1395)	71.9 (69.5 to 74.3)	76.0 (73.7 to 78.2)		
Serotype 6A (n =1403, 1390)	88.9 (87.1 to 90.5)	90.9 (89.2 to 92.3)		
Serotype 6B (n =1413, 1401)	90.5 (88.9 to 92.0)	91.6 (90.0 to 93.0)		
Serotype 7F (n =1409, 1391)	89.1 (87.3 to 90.7)	91.3 (89.7 to 92.7)		
Serotype 9V (n =1399, 1391)	89.1 (87.4 to 90.7)	90.3 (88.6 to 91.8)		
Serotype 14 (n =1418, 1408)	91.6 (90.0 to 93.0)	93.5 (92.1 to 94.8)		
Serotype 18C (n =1420, 1403)	93.8 (92.4 to 95.0)	94.7 (93.4 to 95.8)		
Serotype 19A (n =1420, 1398)	96.3 (95.2 to 97.3)	96.6 (95.5 to 97.5)		
Serotype 19F (n =1421, 1403)	80.3 (78.1 to 82.3)	81.5 (79.3 to 83.5)		
Serotype 23F (n =1424, 1409)	82.1 (80.0 to 84.1)	83.7 (81.6 to 85.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Pneumococcal OPA Titers >=LLOQ for the 7 Additional Serotypes at 1 Month After Vaccination 1 (20vPnC) or 1 Month After Vaccination 2 (PPSV23) in Cohort 1: Evaluable 7-Additional Immunogenicity Population

End point title	Percentage of Subjects With Pneumococcal OPA Titers >=LLOQ for the 7 Additional Serotypes at 1 Month After Vaccination 1 (20vPnC) or 1 Month After Vaccination 2 (PPSV23) in Cohort 1: Evaluable 7-Additional Immunogenicity Population[76]

End point description:

The percentage of subjects with OPA titers >=LLOQ along with corresponding 2-sided 95% CIs were calculated 1 month after vaccination for pneumococcal serotypes 8, 10A, 11A, 12F, 15B, 22F and 33F. E7-AIP included subjects who were enrolled in appropriate cohort based on age, received 20vPnC if randomized to 20vPnC/saline group or received both vaccinations if randomized to 13vPnC/PPSV23 group, had at least 1 valid OPA titers for any of 7 additional serotypes from blood collection 27 to 49 days after Vaccination 1 or Vaccination 2 respectively, had no other major protocol deviations. Here, "n" =subjects evaluable for this endpoint at specified rows.

End point type	Secondary

End point timeframe:

1 month after Vaccination 1 in “Cohort 1: 20vPnC/Saline” or 1 month after Vaccination 2 in “Cohort 1: 13vPnC/PPSV23”

Notes:

[76] - 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 for reporting arms “Cohort 1: 20vPnC/Saline” and “Cohort 1: 13vPnC/PPSV23” only.

End point values	Cohort 1: 20vPnC/Saline	Cohort 1: 13vPnC/PPSV23		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1433	1383		
Units: Percentage of subjects				
number (confidence interval 95%)				
Serotype 8 (n =1374, 1319)	92.9 (91.5 to 94.2)	96.6 (95.5 to 97.5)		
Serotype 10A (n =1310, 1263)	95.6 (94.3 to 96.6)	88.9 (87.1 to 90.6)		
Serotype 11A (n =1198, 1209)	97.7 (96.6 to 98.4)	95.4 (94.0 to 96.5)		
Serotype 12F (n =1294, 1222)	95.7 (94.4 to 96.7)	89.3 (87.4 to 91.0)		
Serotype 15B (n =1283, 1249)	94.1 (92.6 to 95.3)	83.3 (81.1 to 85.3)		
Serotype 22F (n =1274, 1227)	98.6 (97.8 to 99.2)	94.5 (93.0 to 95.7)		
Serotype 33F (n =1157, 1201)	96.4 (95.1 to 97.4)	92.8 (91.2 to 94.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Pneumococcal OPA Titers >=LLOQ for the 20 Vaccines Serotypes at 1 Month After Vaccination (20vPnC) in Cohort 2 and 3: Evaluable-20 Immunogenicity Population

End point title	Percentage of Subjects With Pneumococcal OPA Titers >=LLOQ for the 20 Vaccines Serotypes at 1 Month After Vaccination (20vPnC) in Cohort 2 and 3: Evaluable-20 Immunogenicity Population[77]

End point description:

The percentage of subjects with OPA titers >=LLOQ along with corresponding 2-sided 95% CIs were calculated 1 month after vaccination for pneumococcal serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F, 8, 10A, 11A, 12F, 15B, 22F and 33F. Data for this outcome measure were planned to be analyzed for the 20vPnC groups of Cohorts 2 and 3 only. Evaluable-20 immunogenicity population included subjects who were enrolled in the appropriate cohort based on age, received the vaccination as randomized, had at least 1 valid OPA titer from the blood collection 27 to 49 days after 20vPnC, had no other major protocol deviations. Here, "n" =subjects evaluable for this endpoint at specified rows.

End point type	Secondary

End point timeframe:

1 month after vaccination

Notes:

[77] - 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 for reporting arms "Cohort 1: 20vPnC/Saline" and "Cohort 1: 13vPnC/PPSV23" only.

End point values	Cohort 2: 20vPnC	Cohort 3: 20vPnC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	321	317		
Units: Percentage of subjects				
number (confidence interval 95%)				
Serotype 1 (n =320, 316)	87.2 (83.0 to 90.6)	92.1 (88.5 to 94.8)		
Serotype 3 (n =318, 316)	87.4 (83.3 to 90.9)	89.9 (86.0 to 93.0)		
Serotype 4 (n =318, 315)	94.0 (90.8 to 96.4)	98.1 (95.9 to 99.3)		
Serotype 5 (n =313, 317)	72.8 (67.6 to 77.7)	81.1 (76.3 to 85.2)		
Serotype 6A (n =318, 315)	91.8 (88.2 to 94.6)	99.7 (98.2 to 100.0)		
Serotype 6B (n =318, 314)	95.3 (92.3 to 97.3)	99.0 (97.2 to 99.8)		
Serotype 7F (n =313, 311)	92.7 (89.2 to 95.3)	93.9 (90.6 to 96.3)		
Serotype 9V (n =312, 315)	92.6 (89.1 to 95.3)	99.0 (97.2 to 99.8)		

Serotype 14 (n =313, 316)	94.9 (91.8 to 97.1)	99.1 (97.3 to 99.8)		
Serotype 18C (n =315, 312)	97.5 (95.1 to 98.9)	98.1 (95.9 to 99.3)		
Serotype 19A (n =318, 312)	98.7 (96.8 to 99.7)	99.7 (98.2 to 100.0)		
Serotype 19F (n =320, 315)	81.9 (77.2 to 85.9)	95.2 (92.3 to 97.3)		
Serotype 23F (n =319, 315)	89.3 (85.4 to 92.5)	96.5 (93.8 to 98.2)		
Serotype 8 (n =314, 306)	92.4 (88.8 to 95.0)	95.8 (92.8 to 97.7)		
Serotype 10A (n =296, 292)	98.3 (96.1 to 99.4)	100.0 (98.7 to 100.0)		
Serotype 11A (n =271, 263)	97.0 (94.3 to 98.7)	99.6 (97.9 to 100.0)		
Serotype 12F (n =292, 273)	97.9 (95.6 to 99.2)	98.5 (96.3 to 99.6)		
Serotype 15B (n =284, 279)	95.8 (92.7 to 97.8)	96.8 (94.0 to 98.5)		
Serotype 22F (n =284, 273)	98.2 (95.9 to 99.4)	99.6 (98.0 to 100.0)		
Serotype 33F (n =266, 251)	95.9 (92.7 to 97.9)	99.6 (97.8 to 100.0)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Local reactions: within 10 days after Vaccination 1 (systematic assessment), Systemic events: within 7 days after Vaccination 1 (systematic assessment), Non serious AEs: up to 1 month after Vaccination 1, SAEs: up to 6 months after Vaccination 1

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. Safety population was used for the analysis.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.1

Reporting groups

Reporting group title	Cohort 1: 20vPnC/Saline

Reporting group description:

Subjects aged 60 years and above were randomized to receive a single dose of 0.5 milliliter (mL) intramuscular injection of 20-valent pneumococcal vaccine (20vPnC) at Vaccination 1 (Day 1) and a single dose of 0.5 mL intramuscular injection of saline at Vaccination 2 (28 to 42 days after Vaccination 1).

Reporting group title	Cohort 1: 13vPnC/PPSV23

Reporting group description:

Subjects aged 60 years and above were randomized to receive a single dose of 0.5 mL intramuscular injection of 13-valent pneumococcal vaccine (13vPnC) at Vaccination 1 (Day 1) and a single dose of 0.5 mL intramuscular injection of 23-valent pneumococcal polysaccharide vaccine (PPSV23) at Vaccination 2 (28 to 42 days after vaccination 1).

Reporting group title	Cohort 2: 20vPnC

Reporting group description:

Subjects aged 50 through 59 years were randomized to receive a single dose of 0.5 mL intramuscular injection of 20vPnC (Day 1).

Reporting group title	Cohort 2: 13vPnC

Reporting group description:

Subjects aged 50 through 59 years were randomized to receive a single dose of 0.5 mL intramuscular injection of 13vPnC (Day 1).

Reporting group title	Cohort 3: 20vPnC

Reporting group description:

Subjects aged 18 through 49 years were randomized to receive a single dose of 0.5 mL intramuscular injection of 20vPnC (Day 1).

Reporting group title	Cohort 3: 13vPnC

Reporting group description:

Subjects aged 18 through 49 years were randomized to receive a single dose of 0.5 mL intramuscular injection of 13vPnC (Day 1).

Serious adverse events	Cohort 1: 20vPnC/Saline	Cohort 1: 13vPnC/PPSV23	Cohort 2: 20vPnC
Total subjects affected by serious adverse events			
subjects affected / exposed	36 / 1507 (2.39%)	29 / 1490 (1.95%)	1 / 334 (0.30%)
number of deaths (all causes)	1	0	0
number of deaths resulting from	0	0	0

adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colon cancer			
subjects affected / exposed	0 / 1507 (0.00%)	1 / 1490 (0.07%)	0 / 334 (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
Glioblastoma multiforme			
subjects affected / exposed	0 / 1507 (0.00%)	1 / 1490 (0.07%)	0 / 334 (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
Malignant melanoma			
subjects affected / exposed	0 / 1507 (0.00%)	1 / 1490 (0.07%)	0 / 334 (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
Metastases to peritoneum			
subjects affected / exposed	1 / 1507 (0.07%)	0 / 1490 (0.00%)	0 / 334 (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
Pancreatic carcinoma			
subjects affected / exposed	0 / 1507 (0.00%)	1 / 1490 (0.07%)	0 / 334 (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
Prostate cancer			
subjects affected / exposed	2 / 1507 (0.13%)	0 / 1490 (0.00%)	0 / 334 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transitional cell carcinoma			
subjects affected / exposed	1 / 1507 (0.07%)	0 / 1490 (0.00%)	0 / 334 (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
General disorders and administration site conditions			
Chest pain			

subjects affected / exposed	0 / 1507 (0.00%)	1 / 1490 (0.07%)	0 / 334 (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
Hernia			
subjects affected / exposed	1 / 1507 (0.07%)	0 / 1490 (0.00%)	0 / 334 (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
Non-cardiac chest pain			
subjects affected / exposed	1 / 1507 (0.07%)	0 / 1490 (0.00%)	0 / 334 (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
Systemic inflammatory response syndrome			
subjects affected / exposed	0 / 1507 (0.00%)	1 / 1490 (0.07%)	0 / 334 (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
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 1507 (0.00%)	1 / 1490 (0.07%)	0 / 334 (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
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 1507 (0.00%)	1 / 1490 (0.07%)	0 / 334 (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
Dyspnoea			
subjects affected / exposed	2 / 1507 (0.13%)	0 / 1490 (0.00%)	0 / 334 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	0 / 1507 (0.00%)	1 / 1490 (0.07%)	0 / 334 (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

Pulmonary embolism			
subjects affected / exposed	1 / 1507 (0.07%)	0 / 1490 (0.00%)	0 / 334 (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
Pulmonary oedema			
subjects affected / exposed	0 / 1507 (0.00%)	1 / 1490 (0.07%)	0 / 334 (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
Respiratory failure			
subjects affected / exposed	0 / 1507 (0.00%)	1 / 1490 (0.07%)	0 / 334 (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
Psychiatric disorders			
Completed suicide			
subjects affected / exposed	1 / 1507 (0.07%)	0 / 1490 (0.00%)	0 / 334 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Product issues			
Device malfunction			
subjects affected / exposed	0 / 1507 (0.00%)	1 / 1490 (0.07%)	0 / 334 (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
Investigations			
Blood pressure increased			
subjects affected / exposed	0 / 1507 (0.00%)	1 / 1490 (0.07%)	0 / 334 (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
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	1 / 1507 (0.07%)	0 / 1490 (0.00%)	0 / 334 (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
Gun shot wound			

subjects affected / exposed	1 / 1507 (0.07%)	0 / 1490 (0.00%)	0 / 334 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Head injury			
subjects affected / exposed	1 / 1507 (0.07%)	0 / 1490 (0.00%)	0 / 334 (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
Heat exhaustion			
subjects affected / exposed	1 / 1507 (0.07%)	0 / 1490 (0.00%)	0 / 334 (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
Humerus fracture			
subjects affected / exposed	0 / 1507 (0.00%)	1 / 1490 (0.07%)	0 / 334 (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
Meniscus injury			
subjects affected / exposed	0 / 1507 (0.00%)	1 / 1490 (0.07%)	0 / 334 (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
Muscle rupture			
subjects affected / exposed	0 / 1507 (0.00%)	1 / 1490 (0.07%)	0 / 334 (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
Post procedural haematuria			
subjects affected / exposed	0 / 1507 (0.00%)	1 / 1490 (0.07%)	0 / 334 (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
Stress fracture			
subjects affected / exposed	0 / 1507 (0.00%)	1 / 1490 (0.07%)	0 / 334 (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
Cardiac disorders			
Acute myocardial infarction			

subjects affected / exposed	0 / 1507 (0.00%)	1 / 1490 (0.07%)	0 / 334 (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
Atrial fibrillation			
subjects affected / exposed	1 / 1507 (0.07%)	1 / 1490 (0.07%)	0 / 334 (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
Cardiac failure congestive			
subjects affected / exposed	0 / 1507 (0.00%)	2 / 1490 (0.13%)	0 / 334 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	3 / 1507 (0.20%)	1 / 1490 (0.07%)	0 / 334 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	1 / 1507 (0.07%)	0 / 1490 (0.00%)	0 / 334 (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
Silent myocardial infarction			
subjects affected / exposed	0 / 1507 (0.00%)	1 / 1490 (0.07%)	0 / 334 (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
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	1 / 1507 (0.07%)	0 / 1490 (0.00%)	0 / 334 (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
Hepatic encephalopathy			
subjects affected / exposed	1 / 1507 (0.07%)	0 / 1490 (0.00%)	0 / 334 (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
Ischaemic stroke			

subjects affected / exposed	1 / 1507 (0.07%)	0 / 1490 (0.00%)	0 / 334 (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
Syncope			
subjects affected / exposed	1 / 1507 (0.07%)	1 / 1490 (0.07%)	0 / 334 (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
Transient ischaemic attack			
subjects affected / exposed	1 / 1507 (0.07%)	0 / 1490 (0.00%)	0 / 334 (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
Blood and lymphatic system disorders			
Blood loss anaemia			
subjects affected / exposed	0 / 1507 (0.00%)	1 / 1490 (0.07%)	0 / 334 (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
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	0 / 1507 (0.00%)	1 / 1490 (0.07%)	0 / 334 (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
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 1507 (0.00%)	1 / 1490 (0.07%)	0 / 334 (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
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 1507 (0.00%)	1 / 1490 (0.07%)	0 / 334 (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
Hepatobiliary disorders			
Biloma			
subjects affected / exposed	1 / 1507 (0.07%)	0 / 1490 (0.00%)	0 / 334 (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

Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	2 / 1507 (0.13%)	0 / 1490 (0.00%)	0 / 334 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
End stage renal disease			
subjects affected / exposed	0 / 1507 (0.00%)	1 / 1490 (0.07%)	0 / 334 (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
Haematuria			
subjects affected / exposed	1 / 1507 (0.07%)	0 / 1490 (0.00%)	0 / 334 (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
Renal failure			
subjects affected / exposed	1 / 1507 (0.07%)	0 / 1490 (0.00%)	0 / 334 (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
Nephrolithiasis			
subjects affected / exposed	0 / 1507 (0.00%)	0 / 1490 (0.00%)	1 / 334 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ureteric obstruction			
subjects affected / exposed	0 / 1507 (0.00%)	0 / 1490 (0.00%)	1 / 334 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 1507 (0.07%)	0 / 1490 (0.00%)	0 / 334 (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
Neck mass			
subjects affected / exposed	0 / 1507 (0.00%)	1 / 1490 (0.07%)	0 / 334 (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

Osteoarthritis			
subjects affected / exposed	2 / 1507 (0.13%)	0 / 1490 (0.00%)	0 / 334 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rhabdomyolysis			
subjects affected / exposed	1 / 1507 (0.07%)	0 / 1490 (0.00%)	0 / 334 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	2 / 1507 (0.13%)	0 / 1490 (0.00%)	0 / 334 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis infective			
subjects affected / exposed	1 / 1507 (0.07%)	0 / 1490 (0.00%)	0 / 334 (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
Cellulitis			
subjects affected / exposed	2 / 1507 (0.13%)	1 / 1490 (0.07%)	0 / 334 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			
subjects affected / exposed	1 / 1507 (0.07%)	0 / 1490 (0.00%)	0 / 334 (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
Erysipelas			
subjects affected / exposed	1 / 1507 (0.07%)	0 / 1490 (0.00%)	0 / 334 (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
Diverticulitis			
subjects affected / exposed	0 / 1507 (0.00%)	1 / 1490 (0.07%)	0 / 334 (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
Kidney infection			

subjects affected / exposed	0 / 1507 (0.00%)	1 / 1490 (0.07%)	0 / 334 (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
Skin bacterial infection			
subjects affected / exposed	0 / 1507 (0.00%)	0 / 1490 (0.00%)	0 / 334 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes simplex meningitis			
subjects affected / exposed	0 / 1507 (0.00%)	0 / 1490 (0.00%)	0 / 334 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 1507 (0.00%)	1 / 1490 (0.07%)	0 / 334 (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
Hyperglycaemia			
subjects affected / exposed	0 / 1507 (0.00%)	1 / 1490 (0.07%)	0 / 334 (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
Hyponatraemia			
subjects affected / exposed	1 / 1507 (0.07%)	0 / 1490 (0.00%)	0 / 334 (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
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 1507 (0.00%)	1 / 1490 (0.07%)	0 / 334 (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

Serious adverse events	Cohort 2: 13vPnC	Cohort 3: 20vPnC	Cohort 3: 13vPnC
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 111 (0.90%)	2 / 335 (0.60%)	1 / 112 (0.89%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colon cancer			
subjects affected / exposed	0 / 111 (0.00%)	0 / 335 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Glioblastoma multiforme			
subjects affected / exposed	0 / 111 (0.00%)	0 / 335 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant melanoma			
subjects affected / exposed	0 / 111 (0.00%)	0 / 335 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to peritoneum			
subjects affected / exposed	0 / 111 (0.00%)	0 / 335 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatic carcinoma			
subjects affected / exposed	0 / 111 (0.00%)	0 / 335 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			
subjects affected / exposed	0 / 111 (0.00%)	0 / 335 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transitional cell carcinoma			
subjects affected / exposed	0 / 111 (0.00%)	0 / 335 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			

subjects affected / exposed	0 / 111 (0.00%)	0 / 335 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hernia			
subjects affected / exposed	0 / 111 (0.00%)	0 / 335 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	0 / 111 (0.00%)	0 / 335 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Systemic inflammatory response syndrome			
subjects affected / exposed	0 / 111 (0.00%)	0 / 335 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 111 (0.00%)	0 / 335 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 111 (0.00%)	0 / 335 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 111 (0.00%)	0 / 335 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	0 / 111 (0.00%)	0 / 335 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pulmonary embolism			
subjects affected / exposed	0 / 111 (0.00%)	1 / 335 (0.30%)	0 / 112 (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
Pulmonary oedema			
subjects affected / exposed	0 / 111 (0.00%)	0 / 335 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 111 (0.00%)	0 / 335 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Completed suicide			
subjects affected / exposed	0 / 111 (0.00%)	0 / 335 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Device malfunction			
subjects affected / exposed	0 / 111 (0.00%)	0 / 335 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Blood pressure increased			
subjects affected / exposed	0 / 111 (0.00%)	0 / 335 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	0 / 111 (0.00%)	0 / 335 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gun shot wound			

subjects affected / exposed	0 / 111 (0.00%)	0 / 335 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Head injury			
subjects affected / exposed	0 / 111 (0.00%)	0 / 335 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Heat exhaustion			
subjects affected / exposed	0 / 111 (0.00%)	0 / 335 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus fracture			
subjects affected / exposed	0 / 111 (0.00%)	0 / 335 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meniscus injury			
subjects affected / exposed	0 / 111 (0.00%)	0 / 335 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscle rupture			
subjects affected / exposed	0 / 111 (0.00%)	0 / 335 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haematuria			
subjects affected / exposed	0 / 111 (0.00%)	0 / 335 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stress fracture			
subjects affected / exposed	0 / 111 (0.00%)	0 / 335 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			

subjects affected / exposed	0 / 111 (0.00%)	1 / 335 (0.30%)	0 / 112 (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
Atrial fibrillation			
subjects affected / exposed	0 / 111 (0.00%)	0 / 335 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	0 / 111 (0.00%)	0 / 335 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	0 / 111 (0.00%)	0 / 335 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 111 (0.00%)	0 / 335 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Silent myocardial infarction			
subjects affected / exposed	0 / 111 (0.00%)	0 / 335 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 111 (0.00%)	0 / 335 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic encephalopathy			
subjects affected / exposed	0 / 111 (0.00%)	0 / 335 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			

subjects affected / exposed	0 / 111 (0.00%)	0 / 335 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 111 (0.00%)	0 / 335 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 111 (0.00%)	0 / 335 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Blood loss anaemia			
subjects affected / exposed	0 / 111 (0.00%)	0 / 335 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	0 / 111 (0.00%)	0 / 335 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 111 (0.00%)	0 / 335 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 111 (0.00%)	0 / 335 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Biloma			
subjects affected / exposed	0 / 111 (0.00%)	0 / 335 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 111 (0.00%)	0 / 335 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
End stage renal disease			
subjects affected / exposed	0 / 111 (0.00%)	0 / 335 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematuria			
subjects affected / exposed	0 / 111 (0.00%)	0 / 335 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
subjects affected / exposed	0 / 111 (0.00%)	0 / 335 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	0 / 111 (0.00%)	0 / 335 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ureteric obstruction			
subjects affected / exposed	0 / 111 (0.00%)	0 / 335 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 111 (0.00%)	0 / 335 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neck mass			
subjects affected / exposed	0 / 111 (0.00%)	0 / 335 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Osteoarthritis			
subjects affected / exposed	0 / 111 (0.00%)	0 / 335 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rhabdomyolysis			
subjects affected / exposed	0 / 111 (0.00%)	0 / 335 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 111 (0.00%)	0 / 335 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis infective			
subjects affected / exposed	0 / 111 (0.00%)	0 / 335 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 111 (0.00%)	0 / 335 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			
subjects affected / exposed	0 / 111 (0.00%)	0 / 335 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	0 / 111 (0.00%)	0 / 335 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 111 (0.00%)	0 / 335 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Kidney infection			

subjects affected / exposed	0 / 111 (0.00%)	0 / 335 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin bacterial infection			
subjects affected / exposed	1 / 111 (0.90%)	0 / 335 (0.00%)	0 / 112 (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
Herpes simplex meningitis			
subjects affected / exposed	0 / 111 (0.00%)	0 / 335 (0.00%)	1 / 112 (0.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 111 (0.00%)	0 / 335 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
subjects affected / exposed	0 / 111 (0.00%)	0 / 335 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	0 / 111 (0.00%)	0 / 335 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 111 (0.00%)	0 / 335 (0.00%)	0 / 112 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Cohort 1: 20vPnC/Saline	Cohort 1: 13vPnC/PPSV23	Cohort 2: 20vPnC
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1074 / 1507 (71.27%)	1063 / 1490 (71.34%)	281 / 334 (84.13%)
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 1507 (0.00%)	0 / 1490 (0.00%)	4 / 334 (1.20%)
occurrences (all)	0	0	4
Nervous system disorders			
Headache (HEADACHE)			
subjects affected / exposed	324 / 1507 (21.50%)	345 / 1490 (23.15%)	107 / 334 (32.04%)
occurrences (all)	324	345	107
General disorders and administration site conditions			
Fatigue (FATIGUE)			
subjects affected / exposed	454 / 1507 (30.13%)	455 / 1490 (30.54%)	130 / 334 (38.92%)
occurrences (all)	454	455	130
Injection site erythema (REDNESS)			
subjects affected / exposed	110 / 1507 (7.30%)	92 / 1490 (6.17%)	27 / 334 (8.08%)
occurrences (all)	110	92	27
Injection site pain (PAIN)			
subjects affected / exposed	834 / 1507 (55.34%)	803 / 1490 (53.89%)	240 / 334 (71.86%)
occurrences (all)	834	803	240
Injection site swelling (SWELLING)			
subjects affected / exposed	113 / 1507 (7.50%)	118 / 1490 (7.92%)	29 / 334 (8.68%)
occurrences (all)	113	118	29
Pyrexia (FEVER)			
subjects affected / exposed	0 / 1507 (0.00%)	0 / 1490 (0.00%)	5 / 334 (1.50%)
occurrences (all)	0	0	5
Musculoskeletal and connective tissue disorders			
Arthralgia (JOINT PAIN)			
subjects affected / exposed	190 / 1507 (12.61%)	203 / 1490 (13.62%)	51 / 334 (15.27%)
occurrences (all)	190	203	51
Myalgia (MUSCLE PAIN)			
subjects affected / exposed	588 / 1507 (39.02%)	553 / 1490 (37.11%)	165 / 334 (49.40%)
occurrences (all)	588	553	165

Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	0 / 1507 (0.00%)	0 / 1490 (0.00%)	4 / 334 (1.20%)
occurrences (all)	0	0	4
Influenza			
subjects affected / exposed	0 / 1507 (0.00%)	0 / 1490 (0.00%)	0 / 334 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 1507 (0.00%)	0 / 1490 (0.00%)	0 / 334 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 1507 (0.00%)	0 / 1490 (0.00%)	0 / 334 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Cohort 2: 13vPnC	Cohort 3: 20vPnC	Cohort 3: 13vPnC
Total subjects affected by non-serious adverse events			
subjects affected / exposed	91 / 111 (81.98%)	302 / 335 (90.15%)	107 / 112 (95.54%)
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 111 (0.00%)	0 / 335 (0.00%)	0 / 112 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache (HEADACHE)			
subjects affected / exposed	40 / 111 (36.04%)	130 / 335 (38.81%)	38 / 112 (33.93%)
occurrences (all)	40	130	38
General disorders and administration site conditions			
Fatigue (FATIGUE)			
subjects affected / exposed	40 / 111 (36.04%)	143 / 335 (42.69%)	49 / 112 (43.75%)
occurrences (all)	40	143	49
Injection site erythema (REDNESS)			
subjects affected / exposed	6 / 111 (5.41%)	30 / 335 (8.96%)	11 / 112 (9.82%)
occurrences (all)	6	30	11
Injection site pain (PAIN)			
subjects affected / exposed	77 / 111 (69.37%)	272 / 335 (81.19%)	92 / 112 (82.14%)
occurrences (all)	77	272	92
Injection site swelling (SWELLING)			

subjects affected / exposed	12 / 111 (10.81%)	39 / 335 (11.64%)	14 / 112 (12.50%)
occurrences (all)	12	39	14
Pyrexia (FEVER)			
subjects affected / exposed	1 / 111 (0.90%)	4 / 335 (1.19%)	2 / 112 (1.79%)
occurrences (all)	1	4	2
Musculoskeletal and connective tissue disorders			
Arthralgia (JOINT PAIN)			
subjects affected / exposed	23 / 111 (20.72%)	45 / 335 (13.43%)	20 / 112 (17.86%)
occurrences (all)	23	45	20
Myalgia (MUSCLE PAIN)			
subjects affected / exposed	55 / 111 (49.55%)	223 / 335 (66.57%)	83 / 112 (74.11%)
occurrences (all)	55	223	83
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	3 / 111 (2.70%)	7 / 335 (2.09%)	1 / 112 (0.89%)
occurrences (all)	3	7	1
Influenza			
subjects affected / exposed	0 / 111 (0.00%)	7 / 335 (2.09%)	1 / 112 (0.89%)
occurrences (all)	0	7	1
Nasopharyngitis			
subjects affected / exposed	0 / 111 (0.00%)	6 / 335 (1.79%)	2 / 112 (1.79%)
occurrences (all)	0	6	2
Urinary tract infection			
subjects affected / exposed	0 / 111 (0.00%)	1 / 335 (0.30%)	2 / 112 (1.79%)
occurrences (all)	0	1	2

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 September 2018	1. Revised the scope of clinical assessment, allowing for physical examination based on medical history. 2. Added instruction for the investigator to contact the sponsor or designee for SAEs occurring within 30 days after vaccination

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported