Clinical trial results:
A Phase 3, Multicenter, Randomized, Double-blind, Active-Comparator-controlled Study to Evaluate the Safety, Tolerability, and Immunogenicity of V114 in Healthy Japanese Infants

Summary

EudraCT number	2019-003644-68
Trial protocol	Outside EU/EEA
Global end of trial date	09 February 2022

Results information

Result version number	v1
This version publication date	24 July 2022
First version publication date	24 July 2022

Trial information

Trial identification

Sponsor protocol code	V114-033

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04384107
WHO universal trial number (UTN)	-
Other trial identifiers	JAPIC-CTI: 205287

Notes:

Sponsors

Sponsor organisation name	Merck Sharp & Dohme LLC
Sponsor organisation address	126 East Lincoln Avenue, P.O. Box 2000, Rahway, NJ, United States, 07065
Public contact	Clinical Trials Disclosure, Merck Sharp & Dohme LLC, ClinicalTrialsDisclosure@merck.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme LLC, ClinicalTrialsDisclosure@merck.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	01 December 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 December 2021
Global end of trial reached?	Yes
Global end of trial date	09 February 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this clinical study is to evaluate the safety and immunogenicity of a 4-dose schedule (3-dose primary series followed by a toddler dose) of V114 compared with Pneumococcal 13-valent Conjugate Vaccine (PCV13). The hypotheses are that: 1) V114 is non-inferior to PCV13 for the 13 shared serotypes between V114 and PCV13 based on the response rates at 30 days following dose 3; 2) V114 is non-inferior to PCV13 for the 2 unique V114 serotypes based on the response rate of the 2 unique V114 serotypes at 30 days following dose 3; 3) V114 is non-inferior to PCV13 for the 13 shared serotypes between V114 and PCV13 based on anti-pneumococcal polysaccharide (PnPs) serotype-specific Immunoglobulin G (IgG) geometric mean concentrations (GMCs) at 30 days following dose 3.

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 July 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Japan: 694
Worldwide total number of subjects	694
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	694
Children (2-11 years)	0
Adolescents (12-17 years)	0

Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study enrolled healthy Japanese infants at 2 to 6 months of age.

Pre-assignment

Screening details:

694 infants were randomized in a 1:1 ratio with stratification into 3 categories by age category (2 months, 3 months and 4 to 6 months of age), to receive either V114 or PCV13.

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, Subject, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	V114

Arm description:

Participants received single 0.5 mL subcutaneous injection of V114 administered at 2 to 6 months of age, and second and third dose is administered at an interval of ≥27 days from the prior dose. The fourth dose is administered at 12 to 15 months of age.

Arm type	Experimental
Investigational medicinal product name	V114
Investigational medicinal product code	
Other name	Pneumococcal 15-valent Conjugate Vaccine, VAXNEUVANCE™
Pharmaceutical forms	Suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

15-valent pneumococcal conjugate vaccine containing 13 serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F) present in Prevnar 13™ plus 2 additional serotypes (22F, 33F) in each 0.5 mL dose

Arm title	PCV13

Arm description:

Participants received a single 0.5 mL subcutaneous injection of PCV13 administered at 2 to 6 months of age, and second and third dose is administered at an interval of ≥27 days from the prior dose. The fourth dose is administered at 12 to 15 months of age.

Arm type	Experimental
Investigational medicinal product name	PCV13
Investigational medicinal product code	
Other name	Prevnar 13™
Pharmaceutical forms	Suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

13-valent pneumococcal conjugate vaccine containing 13 serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F) in each 0.5 mL dose

Number of subjects in period 1	V114	PCV13
Started	347	347
Dose 1	347	346
Dose 2	344	346
Dose 3	343	346
Dose 4	340	342
Completed	338	341
Not completed	9	6
Withdrawal By Parent/Guardian	8	6
Lost to follow-up	1	-

Baseline characteristics

Reporting groups	
Reporting group title	V114
Reporting group description:	
Participants received single 0.5 mL subcutaneous injection of V114 administered at 2 to 6 months of age, and second and third dose is administered at an interval of ≥27 days from the prior dose. The fourth dose is administered at 12 to 15 months of age.	
Reporting group title	PCV13
Reporting group description:	
Participants received a single 0.5 mL subcutaneous injection of PCV13 administered at 2 to 6 months of age, and second and third dose is administered at an interval of ≥27 days from the prior dose. The fourth dose is administered at 12 to 15 months of age.	

Reporting group values	V114	PCV13	Total
Number of subjects	347	347	694
Age Categorical Units: Subjects			
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	347	347	694
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	2.4	2.4	
standard deviation	± 0.4	± 0.4	-
Gender Categorical Units: Subjects			
Female	166	173	339
Male	181	174	355
Race Units: Subjects			
Asian	347	347	694
Ethnicity Units: Subjects			
Not Hispanic or Latino	347	347	694

End points

End points reporting groups

Reporting group title	V114
Reporting group description:	
Participants received single 0.5 mL subcutaneous injection of V114 administered at 2 to 6 months of age, and second and third dose is administered at an interval of ≥27 days from the prior dose. The fourth dose is administered at 12 to 15 months of age.	
Reporting group title	PCV13
Reporting group description:	
Participants received a single 0.5 mL subcutaneous injection of PCV13 administered at 2 to 6 months of age, and second and third dose is administered at an interval of ≥27 days from the prior dose. The fourth dose is administered at 12 to 15 months of age.	

Primary: Percentage of Participants with Solicited Injection-Site Adverse Events

End point title	Percentage of Participants with Solicited Injection-Site Adverse Events
End point description:	
An adverse event (AE) is any untoward medical occurrence in a patient or clinical study participant, temporally associated with the use of study treatment, whether or not considered related to the study treatment. Following any injection with either V114 or PCV13 the percentage of participants with solicited injection-site AEs was assessed. The solicited injection-site AEs were erythema, induration, pain, and swelling. All randomized participants who received at least 1 dose of study vaccination were analyzed. One participant in the PCV13 group did not receive PCV13 and therefore was not included in the analysis for this end point.	
End point type	Primary
End point timeframe:	
Day 1 to Day 14 post any vaccination	

End point values	V114	PCV13		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	347	346		
Units: Percentage of Participants				
number (not applicable)				
Injection site erythema	88.2	89.3		
Injection site induration	81.0	81.2		
Injection site pain	31.1	24.0		
Injection site swelling	75.8	79.8		

Statistical analyses

Statistical analysis title	Injection site erythema
Comparison groups	PCV13 v V114

Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	= 0.641
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percent
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.9
upper limit	3.6

Notes:

[1] - Estimated differences, confidence intervals (CIs), and p-values are calculated based on the Miettinen & Nurminen method and are provided in accordance with the statistical analysis plan.

Statistical analysis title	Injection site induration
Comparison groups	V114 v PCV13
Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	other[2]
P-value	= 0.937
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percent
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.1
upper limit	5.6

Notes:

[2] - Estimated differences, confidence intervals (CIs), and p-values are calculated based on the Miettinen & Nurminen method and are provided in accordance with the statistical analysis plan.

Statistical analysis title	Injection site pain
Comparison groups	V114 v PCV13
Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	other[3]
P-value	= 0.036
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percent
Point estimate	7.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5
upper limit	13.8

Notes:

[3] - Estimated differences, confidence intervals (CIs), and p-values are calculated based on the Miettinen & Nurminen method and are provided in accordance with the statistical analysis plan.

Statistical analysis title	Injection site swelling

Comparison groups	V114 v PCV13
Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	other[4]
P-value	= 0.208
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percent
Point estimate	-4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.2
upper limit	2.2

Notes:

[4] - Estimated differences, confidence intervals (CIs), and p-values are calculated based on the Miettinen & Nurminen method and are provided in accordance with the statistical analysis plan.

Primary: Percentage of Participants with Solicited Systemic Adverse Events

End point title	Percentage of Participants with Solicited Systemic Adverse Events

End point description:

An AE is any untoward medical occurrence in a patient or clinical study participant, temporally associated with the use of study treatment, whether or not considered related to the study treatment. Following any of the injections with either V114 or PCV13, the percentage of participants with solicited systemic AEs was assessed. The solicited systemic AEs assessed were decreased appetite, irritability, somnolence, and urticaria. All randomized participants who received at least 1 dose of study vaccination were analyzed. One participant in the PCV13 group did not receive PCV13 and therefore was not included in the analysis for this end point.

End point type	Primary

End point timeframe:

Day 1 to Day 14 post any vaccination

End point values	V114	PCV13		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	347	346		
Units: Percentage of Participants				
number (not applicable)				
Decreased appetite	23.9	24.3		
Irritability	66.6	60.7		
Somnolence	55.9	54.9		
Urticaria	4.0	4.3		

Statistical analyses

Statistical analysis title	Decreased appetite
Comparison groups	V114 v PCV13

Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	other[5]
P-value	= 0.912
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percent
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.7
upper limit	6

Notes:

[5] - Estimated differences, confidence intervals (CIs), and p-values are calculated based on the Miettinen & Nurminen method and are provided in accordance with the statistical analysis plan.

Statistical analysis title	Irritability
Comparison groups	V114 v PCV13
Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	other[6]
P-value	= 0.108
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percent
Point estimate	5.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	13

Notes:

[6] - Estimated differences, confidence intervals (CIs), and p-values are calculated based on the Miettinen & Nurminen method and are provided in accordance with the statistical analysis plan.

Statistical analysis title	Somnolence
Comparison groups	V114 v PCV13
Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	other[7]
P-value	= 0.792
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percent
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.4
upper limit	8.4

Notes:

[7] - Estimated differences, confidence intervals (CIs), and p-values are calculated based on the Miettinen & Nurminen method and are provided in accordance with the statistical analysis plan.

Statistical analysis title	Urticaria

Comparison groups	V114 v PCV13
Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	other[8]
P-value	= 0.843
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percent
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.5
upper limit	2.8

Notes:

[8] - Estimated differences, confidence intervals (CIs), and p-values are calculated based on the Miettinen & Nurminen method and are provided in accordance with the statistical analysis plan.

Primary: Percentage of Participants with Vaccine-Related Serious Adverse Events

End point title	Percentage of Participants with Vaccine-Related Serious Adverse Events

End point description:

A serious adverse event (SAE) is an AE that is life-threatening, requires or prolongs an existing hospitalization, results in persistent or significant disability or incapacity, is a congenital anomaly or birth defect, or is another important medical event deemed such by medical or scientific judgment. The percentage of participants with a vaccine-related SAE following dose 1 (with either V114 or PCV13) was reported. Vaccine-related SAEs were counted starting after vaccine dose 1 through completion of study. All randomized participants who received at least 1 dose of the relevant study vaccination for the timepoint of interest were analyzed. One participant in the PCV13 group did not receive PCV13 and therefore was not included in the analysis for this end point.

End point type	Primary

End point timeframe:

~1 month after Dose 4 (Up to 14 months)

End point values	V114	PCV13		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	347	346		
Units: Percentage of Participants				
number (not applicable)	0.3	0.3		

Statistical analyses

Statistical analysis title	Vaccine-related SAEs

Statistical analysis description:

Estimated differences and CIs are calculated based on the Miettinen & Nurminen method and are provided in accordance with the statistical analysis plan.

Comparison groups	V114 v PCV13

Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percent
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	1.3

Primary: Percentage of Participants Meeting the Serotype Specific Immunoglobulin G Threshold Value of ≥0.35 µg/mL for Each Serotype in V114 After Dose 3

End point title	Percentage of Participants Meeting the Serotype Specific Immunoglobulin G Threshold Value of ≥0.35 µg/mL for Each Serotype in V114 After Dose 3

End point description:

The anti-pneumococcal polysaccharide (PnPs) serotype-specific immunoglobulin G (IgG) response rates (percentage of participants meeting serotype-specific IgG threshold value of ≥0.35 µg/mL of participants administered V114 versus participants administered PCV13) for the 15 serotypes contained in V114 were determined using an electrochemiluminescence assay. All randomized participants without protocol deviations that could have substantially impacted the results of the immunogenicity endpoint and who had sufficient data to perform the analyses were analyzed. One participant in the PCV13 group did not receive PCV13 and therefore was not included in the analysis for this end point.

End point type	Primary

End point timeframe:

30 Days after Dose 3

End point values	V114	PCV13		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	347	346		
Units: Percentage of Participants				
number (not applicable)				
Serotype 1 (Shared) (n=339, 343)	99.7	100.0		
Serotype 3 (Shared) (n=339, 343)	100.0	97.7		
Serotype 4 (Shared) (n=339, 343)	100.0	100.0		
Serotype 5 (Shared) (n=338, 343)	98.8	100.0		
Serotype 6A (Shared) (n=339, 343)	99.1	100.0		
Serotype 6B (Shared) (n=339, 343)	95.0	98.8		
Serotype 7F (Shared) (n=339, 343)	99.7	100.0		
Serotype 9V (Shared) (n=339, 343)	99.7	100.0		
Serotype 14 (Shared) (n=339, 342)	99.4	99.7		
Serotype 18C (Shared) (n=339, 343)	98.8	100.0		
Serotype 19A (Shared) (n=339, 343)	99.7	100.0		
Serotype 19F (Shared) (n=339, 343)	100.0	100.0		
Serotype 23F (Shared) (n=338, 342)	97.9	99.7		
Serotype 22F (Unique to V114) (n=339, 343)	99.7	97.7		

Serotype 33F (Unique to V114) (n=339, 343)	90.9	97.7		

Statistical analyses

Statistical analysis title	Serotype 1
Statistical analysis description: Participants With IgG ≥0.35 µg/mL	
Comparison groups	V114 v PCV13
Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	non-inferiority[9]
P-value	< 0.001
Method	Miettinen and Nurminen
Parameter estimate	Difference in Percent
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.7
upper limit	0.8

Notes:

[9] - The stratum-adjusted proportion difference using the Cochran-Mantel-Haenszel weight, and the corresponding 95% CI and p-value based on the method of Miettinen and Nurminen stratified by age category (2 months of age, ≥3 months of age). A conclusion of non-inferiority of V114 to PCV13 is based on the lower bound of the 2-sided 95% CI for the difference in percentages (V114 - PCV13) being >-10 percentage points (1-sided p-value <0.025).

Statistical analysis title	Serotype 3
Statistical analysis description: Participants With IgG ≥0.35 µg/mL	
Comparison groups	V114 v PCV13
Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	non-inferiority[10]
P-value	< 0.001
Method	Miettinen and Nurminen
Parameter estimate	Difference in Percent
Point estimate	2.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	1
upper limit	4.5

Notes:

[10] - The stratum-adjusted proportion difference using the Cochran-Mantel-Haenszel weight, and the corresponding 95% CI and p-value based on the method of Miettinen and Nurminen stratified by age category (2 months of age, ≥3 months of age). A conclusion of non-inferiority of V114 to PCV13 is based on the lower bound of the 2-sided 95% CI for the difference in percentages (V114 - PCV13) being >-10 percentage points (1-sided p-value <0.025).

Statistical analysis title	Serotype 4
Statistical analysis description:	
Participants With IgG ≥0.35 µg/mL	
Comparison groups	V114 v PCV13
Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	non-inferiority[11]
P-value	< 0.001
Method	Miettinen and Nurminen
Parameter estimate	Difference in Percent
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	1.1

Notes:

[11] - The stratum-adjusted proportion difference using the Cochran-Mantel-Haenszel weight, and the corresponding 95% CI and p-value based on the method of Miettinen and Nurminen stratified by age category (2 months of age, ≥3 months of age). A conclusion of non-inferiority of V114 to PCV13 is based on the lower bound of the 2-sided 95% CI for the difference in percentages (V114 - PCV13) being >-10 percentage points (1-sided p-value <0.025).

Statistical analysis title	Serotype 5
Statistical analysis description:	
Participants With IgG ≥0.35 µg/mL	
Comparison groups	V114 v PCV13
Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	non-inferiority[12]
P-value	< 0.001
Method	Miettinen and Nurminen
Parameter estimate	Difference in Percent
Point estimate	-1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3
upper limit	-0.1

Notes:

[12] - The stratum-adjusted proportion difference using the Cochran-Mantel-Haenszel weight, and the corresponding 95% CI and p-value based on the method of Miettinen and Nurminen stratified by age category (2 months of age, ≥3 months of age). A conclusion of non-inferiority of V114 to PCV13 is based on the lower bound of the 2-sided 95% CI for the difference in percentages (V114 - PCV13) being >-10 percentage points (1-sided p-value <0.025).

Statistical analysis title	Serotype 6A
Statistical analysis description:	
Participants With IgG ≥0.35 µg/mL	
Comparison groups	V114 v PCV13

Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	non-inferiority[13]
P-value	< 0.001
Method	Miettinen and Nurminen
Parameter estimate	Difference in Percent
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.6
upper limit	0.2

Notes:

[13] - The stratum-adjusted proportion difference using the Cochran-Mantel-Haenszel weight, and the corresponding 95% CI and p-value based on the method of Miettinen and Nurminen stratified by age category (2 months of age, ≥3 months of age). A conclusion of non-inferiority of V114 to PCV13 is based on the lower bound of the 2-sided 95% CI for the difference in percentages (V114 - PCV13) being >-10 percentage points (1-sided p-value <0.025).

Statistical analysis title	Serotype 6B
Statistical analysis description:	
Participants With IgG ≥0.35 µg/mL	
Comparison groups	V114 v PCV13
Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	non-inferiority[14]
P-value	< 0.001
Method	Miettinen and Nurminen
Parameter estimate	Difference in Percent
Point estimate	-3.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.9
upper limit	-1.3

Notes:

[14] - The stratum-adjusted proportion difference using the Cochran-Mantel-Haenszel weight, and the corresponding 95% CI and p-value based on the method of Miettinen and Nurminen stratified by age category (2 months of age, ≥3 months of age). A conclusion of non-inferiority of V114 to PCV13 is based on the lower bound of the 2-sided 95% CI for the difference in percentages (V114 - PCV13) being >-10 percentage points (1-sided p-value <0.025).

Statistical analysis title	Serotype 7F
Statistical analysis description:	
Participants With IgG ≥0.35 µg/mL	
Comparison groups	V114 v PCV13
Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	non-inferiority[15]
P-value	< 0.001
Method	Miettinen and Nurminen
Parameter estimate	Difference in Percent
Point estimate	-0.3

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.7
upper limit	0.8

Notes:

[15] - The stratum-adjusted proportion difference using the Cochran-Mantel-Haenszel weight, and the corresponding 95% CI and p-value based on the method of Miettinen and Nurminen stratified by age category (2 months of age, ≥3 months of age). A conclusion of non-inferiority of V114 to PCV13 is based on the lower bound of the 2-sided 95% CI for the difference in percentages (V114 - PCV13) being >-10 percentage points (1-sided p-value <0.025).

Statistical analysis title	Serotype 9V
Statistical analysis description:	
Participants With IgG ≥0.35 µg/mL	
Comparison groups	V114 v PCV13
Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	non-inferiority[16]
P-value	< 0.001
Method	Miettinen and Nurminen
Parameter estimate	Difference in Percent
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.7
upper limit	0.8

Notes:

[16] - The stratum-adjusted proportion difference using the Cochran-Mantel-Haenszel weight, and the corresponding 95% CI and p-value based on the method of Miettinen and Nurminen stratified by age category (2 months of age, ≥3 months of age). A conclusion of non-inferiority of V114 to PCV13 is based on the lower bound of the 2-sided 95% CI for the difference in percentages (V114 - PCV13) being >-10 percentage points (1-sided p-value <0.025).

Statistical analysis title	Serotype 14
Statistical analysis description:	
Participants With IgG ≥0.35 µg/mL	
Comparison groups	V114 v PCV13
Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	non-inferiority[17]
P-value	< 0.001
Method	Miettinen and Nurminen
Parameter estimate	Difference in Percent
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.9
upper limit	1.1

Notes:

[17] - The stratum-adjusted proportion difference using the Cochran-Mantel-Haenszel weight, and the corresponding 95% CI and p-value based on the method of Miettinen and Nurminen stratified by age category (2 months of age, ≥3 months of age). A conclusion of non-inferiority of V114 to PCV13 is

based on the lower bound of the 2-sided 95% CI for the difference in percentages (V114 - PCV13) being >-10 percentage points (1-sided p-value <0.025).

Statistical analysis title	Serotype 18C
Statistical analysis description:	
Participants With IgG ≥0.35 µg/mL	
Comparison groups	V114 v PCV13
Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	non-inferiority[18]
P-value	< 0.001
Method	Miettinen and Nurminen
Parameter estimate	Difference in Percent
Point estimate	-1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3
upper limit	-0.1

Notes:

[18] - The stratum-adjusted proportion difference using the Cochran-Mantel-Haenszel weight, and the corresponding 95% CI and p-value based on the method of Miettinen and Nurminen stratified by age category (2 months of age, ≥3 months of age). A conclusion of non-inferiority of V114 to PCV13 is based on the lower bound of the 2-sided 95% CI for the difference in percentages (V114 - PCV13) being >-10 percentage points (1-sided p-value <0.025).

Statistical analysis title	Serotype 19A
Statistical analysis description:	
Participants With IgG ≥0.35 µg/mL	
Comparison groups	V114 v PCV13
Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	non-inferiority[19]
P-value	< 0.001
Method	Miettinen and Nurminen
Parameter estimate	Difference in Percent
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.7
upper limit	0.8

Notes:

[19] - The stratum-adjusted proportion difference using the Cochran-Mantel-Haenszel weight, and the corresponding 95% CI and p-value based on the method of Miettinen and Nurminen stratified by age category (2 months of age, ≥3 months of age). A conclusion of non-inferiority of V114 to PCV13 is based on the lower bound of the 2-sided 95% CI for the difference in percentages (V114 - PCV13) being >-10 percentage points (1-sided p-value <0.025).

Statistical analysis title	Serotype 19F
Statistical analysis description:	
Participants With IgG ≥0.35 µg/mL	
Comparison groups	V114 v PCV13

Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	non-inferiority[20]
P-value	< 0.001
Method	Miettinen and Nurminen
Parameter estimate	Difference in Percent
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	1.1

Notes:

[20] - The stratum-adjusted proportion difference using the Cochran-Mantel-Haenszel weight, and the corresponding 95% CI and p-value based on the method of Miettinen and Nurminen stratified by age category (2 months of age, ≥3 months of age). A conclusion of non-inferiority of V114 to PCV13 is based on the lower bound of the 2-sided 95% CI for the difference in percentages (V114 - PCV13) being >-10 percentage points (1-sided p-value <0.025).

Statistical analysis title	Serotype 23F
Statistical analysis description:	
Participants With IgG ≥0.35 µg/mL	
Comparison groups	V114 v PCV13
Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	non-inferiority[21]
P-value	< 0.001
Method	Miettinen and Nurminen
Parameter estimate	Difference in Percent
Point estimate	-1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4
upper limit	-0.2

Notes:

[21] - The stratum-adjusted proportion difference using the Cochran-Mantel-Haenszel weight, and the corresponding 95%
CI and p-value based on the method of Miettinen and Nurminen stratified by age category (2 months of age, ≥3
months of age). A conclusion of non-inferiority of V114 to PCV13 is based on the lower bound of the 2-sided 95% CI for the difference in percentages (V114 - PCV13) being >-10 percentage points (1-sided p-value <0.025).

Statistical analysis title	Serotype 22F
Statistical analysis description:	
Participants With IgG ≥0.35 µg/mL	
Comparison groups	V114 v PCV13
Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	non-inferiority[22]
P-value	< 0.001
Method	Miettinen and Nurminen
Parameter estimate	Difference in Percent
Point estimate	2

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.4
upper limit	4.3

Notes:

[22] - The stratum-adjusted proportion difference using the Cochran-Mantel-Haenszel weight, and the corresponding 95% CI and p-value based on the method of Miettinen and Nurminen stratified by age category (2 months of age, ≥3 months of age). A conclusion of non-inferiority of V114 to PCV13 is based on the lower bound of the 2-sided 95% CI for the difference in percentages (V114 - PCV13) being >-10 percentage points (1-sided p-value <0.025).

Statistical analysis title	Serotype 33F

Statistical analysis description:

Participants With IgG ≥0.35 µg/mL

Comparison groups	V114 v PCV13
Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	non-inferiority[23]
P-value	= 0.048
Method	Miettinen and Nurminen
Parameter estimate	Difference in Percent
Point estimate	-6.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.6
upper limit	-3.5

Notes:

[23] - The stratum-adjusted proportion difference using the Cochran-Mantel-Haenszel weight, and the corresponding 95% CI and p-value based on the method of Miettinen and Nurminen stratified by age category (2 months of age, ≥3 months of age). A conclusion of non-inferiority of V114 to PCV13 is based on the lower bound of the 2-sided 95% CI for the difference in percentages (V114 - PCV13) being >-10 percentage points (1-sided p-value <0.025).

Primary: Geometric Mean Concentration of Serotype-Specific IgG for the 13 Shared Serotypes in V114 and PCV13 After Dose 3

End point title	Geometric Mean Concentration of Serotype-Specific IgG for the 13 Shared Serotypes in V114 and PCV13 After Dose 3

End point description:

The anti-PnPs serotype-specific IgG Geometric Mean Concentrations (GMCs) of participants administered V114 versus participants administered PCV13 for the 13 serotypes shared in V114 and PCV13 were determined using an electrochemiluminescence assay. All randomized participants without protocol deviations that could have substantially impacted the results of the immunogenicity endpoint and who had sufficient data to perform the analyses were analyzed. One participant in the PCV13 group did not receive PCV13 and therefore was not included in the analysis for this end point.

End point type	Primary

End point timeframe:

30 Days after Dose 3

End point values	V114	PCV13		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	347	346		
Units: µg/mL				
geometric mean (confidence interval 95%)				
Serotype 1 (Shared) (n=339, 343)	2.39 (2.19 to 2.62)	3.95 (3.61 to 4.32)		
Serotype 3 (Shared) (n=339, 343)	2.63 (2.39 to 2.89)	1.42 (1.29 to 1.56)		
Serotype 4 (Shared) (n=339, 343)	2.98 (2.71 to 3.27)	3.54 (3.23 to 3.89)		
Serotype 5 (Shared) (n=338, 343)	2.59 (2.32 to 2.89)	3.35 (3.00 to 3.74)		
Serotype 6A (Shared) (n=339, 343)	2.51 (2.26 to 2.79)	4.45 (4.00 to 4.94)		
Serotype 6B (Shared) (n=339, 343)	2.46 (2.14 to 2.82)	4.17 (3.63 to 4.79)		
Serotype 7F (Shared) (n=339, 343)	4.38 (3.95 to 4.85)	5.22 (4.71 to 5.78)		
Serotype 9V (Shared) (n=339, 343)	3.09 (2.80 to 3.41)	3.55 (3.22 to 3.92)		
Serotype 14 (Shared) (n=339, 342)	8.99 (7.96 to 10.14)	12.03 (10.66 to 13.57)		
Serotype 18C (Shared) (n=339, 343)	2.85 (2.58 to 3.14)	3.85 (3.49 to 4.25)		
Serotype 19A (Shared) (n=339, 343)	3.44 (3.14 to 3.77)	5.28 (4.82 to 5.79)		
Serotype 19F (Shared) (n=339, 343)	4.24 (3.93 to 4.58)	5.65 (5.24 to 6.10)		
Serotype 23F (Shared) (n=338, 342)	2.42 (2.15 to 2.72)	2.95 (2.62 to 3.32)		

Statistical analyses

Statistical analysis title	Serotype 1
Statistical analysis description: IgG GMC Ratio	
Comparison groups	V114 v PCV13
Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	non-inferiority[24]
P-value	< 0.001
Method	Linear model
Parameter estimate	GMC Ratio
Point estimate	0.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.55
upper limit	0.67

Notes:

[24] - Based on a linear model with natural log-transformed IgG concentrations as response variable, and vaccination group and age category (2 months of age, ≥3 months of age) as factors. A conclusion of non-inferiority of V114 to PCV13 is based on the lower bound of the 2-sided 95% CI for the GMC ratio (V114/PCV13) being >0.5 (1-sided p-value <0.025).

Statistical analysis title	Serotype 3
Statistical analysis description:	
IgG GMC Ratio	
Comparison groups	V114 v PCV13
Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	non-inferiority[25]
P-value	< 0.001
Method	Linear model
Parameter estimate	GMC Ratio
Point estimate	1.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.67
upper limit	2.05

Notes:

[25] - Based on a linear model with natural log-transformed IgG concentrations as response variable, and vaccination group and age category (2 months of age, ≥3 months of age) as factors. A conclusion of non-inferiority of V114 to PCV13 is based on the lower bound of the 2-sided 95% CI for the GMC ratio (V114/PCV13) being >0.5 (1-sided p-value <0.025).

Statistical analysis title	Serotype 4
Statistical analysis description:	
IgG GMC Ratio	
Comparison groups	V114 v PCV13
Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	non-inferiority[26]
P-value	< 0.001
Method	Linear model
Parameter estimate	GMC Ratio
Point estimate	0.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.76
upper limit	0.93

Notes:

[26] - Based on a linear model with natural log-transformed IgG concentrations as response variable, and vaccination group and age category (2 months of age, ≥3 months of age) as factors. A conclusion of non-inferiority of V114 to PCV13 is based on the lower bound of the 2-sided 95% CI for the GMC ratio (V114/PVC 13) being >0.5 (1-sided p-value <0.025).

Statistical analysis title	Serotype 5
Statistical analysis description:	
IgG GMC Ratio	
Comparison groups	V114 v PCV13

Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	non-inferiority[27]
P-value	< 0.001
Method	Linear model
Parameter estimate	GMC Ratio
Point estimate	0.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.69
upper limit	0.87

Notes:

[27] - Based on a linear model with natural log-transformed IgG concentrations as response variable, and vaccination group and age category (2 months of age, ≥3 months of age) as factors. A conclusion of non-inferiority of V114 to PCV13 is based on the lower bound of the 2-sided 95% CI for the GMC ratio (V114/PVC 13) being >0.5 (1-sided p-value <0.025).

Statistical analysis title	Serotype 6A
Statistical analysis description:	
IgG GMC Ratio	
Comparison groups	V114 v PCV13
Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	non-inferiority[28]
P-value	= 0.019
Method	Linear model
Parameter estimate	GMC Ratio
Point estimate	0.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5
upper limit	0.63

Notes:

[28] - Based on a linear model with natural log-transformed IgG concentrations as response variable, and vaccination group and age category (2 months of age, ≥3 months of age) as factors. A conclusion of non-inferiority of V114 to PCV13 is based on the lower bound of the 2-sided 95% CI for the GMC ratio (V114/PVC 13) being >0.5 (1-sided p-value <0.025).

Statistical analysis title	Serotype 6B
Statistical analysis description:	
IgG GMC Ratio	
Comparison groups	V114 v PCV13
Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	non-inferiority[29]
P-value	= 0.015
Method	Linear model
Parameter estimate	GMC Ratio
Point estimate	0.59

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.51
upper limit	0.68

Notes:

[29] - Based on a linear model with natural log-transformed IgG concentrations as response variable, and vaccination group and age category (2 months of age, ≥3 months of age) as factors. A conclusion of non-inferiority of V114 to PCV13 is based on the lower bound of the 2-sided 95% CI for the GMC ratio (V114/PVC 13) being >0.5 (1-sided p-value <0.025).

Statistical analysis title	Serotype 7F

Statistical analysis description:

IgG GMC Ratio

Comparison groups	V114 v PCV13
Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	non-inferiority[30]
P-value	< 0.001
Method	Linear model
Parameter estimate	GMC Ratio
Point estimate	0.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.75
upper limit	0.94

Notes:

[30] - Based on a linear model with natural log-transformed IgG concentrations as response variable, and vaccination group and age category (2 months of age, ≥3 months of age) as factors. A conclusion of non-inferiority of V114 to PCV13 is based on the lower bound of the 2-sided 95% CI for the GMC ratio (V114/PVC 13) being >0.5 (1-sided p-value <0.025).

Statistical analysis title	Serotype 9V

Statistical analysis description:

IgG GMC Ratio

Comparison groups	V114 v PCV13
Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	non-inferiority[31]
P-value	< 0.001
Method	Linear model
Parameter estimate	GMC Ratio
Point estimate	0.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.78
upper limit	0.97

Notes:

[31] - Based on a linear model with natural log-transformed IgG concentrations as response variable, and vaccination group and age category (2 months of age, ≥3 months of age) as factors. A conclusion of non-inferiority of V114 to PCV13 is based on the lower bound of the 2-sided 95% CI for the GMC ratio (V114/PVC 13) being >0.5 (1-sided p-value <0.025).

Statistical analysis title	Serotype 14
Statistical analysis description:	
IgG GMC Ratio	
Comparison groups	V114 v PCV13
Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	non-inferiority[32]
P-value	< 0.001
Method	Linear model
Parameter estimate	GMC Ratio
Point estimate	0.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.66
upper limit	0.85

Notes:

[32] - Based on a linear model with natural log-transformed IgG concentrations as response variable, and vaccination group and age category (2 months of age, ≥3 months of age) as factors. A conclusion of non-inferiority of V114 to PCV13 is based on the lower bound of the 2-sided 95% CI for the GMC ratio (V114/PVC 13) being >0.5 (1-sided p-value <0.025).

Statistical analysis title	Serotype 18C
Statistical analysis description:	
IgG GMC Ratio	
Comparison groups	V114 v PCV13
Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	non-inferiority[33]
P-value	< 0.001
Method	Linear model
Parameter estimate	GMC Ratio
Point estimate	0.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.67
upper limit	0.82

Notes:

[33] - Based on a linear model with natural log-transformed IgG concentrations as response variable, and vaccination group and age category (2 months of age, ≥3 months of age) as factors. A conclusion of non-inferiority of V114 to PCV13 is based on the lower bound of the 2-sided 95% CI for the GMC ratio (V114/PVC 13) being >0.5 (1-sided p-value <0.025).

Statistical analysis title	Serotype 19A
Statistical analysis description:	
IgG GMC Ratio	
Comparison groups	V114 v PCV13

Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	non-inferiority[34]
P-value	< 0.001
Method	Linear model
Parameter estimate	GMC Ratio
Point estimate	0.65
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.59
upper limit	0.72

Notes:

[34] - Based on a linear model with natural log-transformed IgG concentrations as response variable, and vaccination group and age category (2 months of age, ≥3 months of age) as factors. A conclusion of non-inferiority of V114 to PCV13 is based on the lower bound of the 2-sided 95% CI for the GMC ratio (V114/PVC 13) being >0.5 (1-sided p-value <0.025).

Statistical analysis title	Serotype 19F
Statistical analysis description:	
IgG GMC Ratio	
Comparison groups	V114 v PCV13
Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	non-inferiority[35]
P-value	< 0.001
Method	Linear model
Parameter estimate	GMC Ratio
Point estimate	0.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.69
upper limit	0.82

Notes:

[35] - Based on a linear model with natural log-transformed IgG concentrations as response variable, and vaccination group and age category (2 months of age, ≥3 months of age) as factors. A conclusion of non-inferiority of V114 to PCV13 is based on the lower bound of the 2-sided 95% CI for the GMC ratio (V114/PVC 13) being >0.5 (1-sided p-value <0.025).

Statistical analysis title	Serotype 23F
Statistical analysis description:	
IgG GMC Ratio	
Comparison groups	V114 v PCV13
Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	non-inferiority[36]
P-value	< 0.001
Method	Linear model
Parameter estimate	GMC Ratio
Point estimate	0.82

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.72
upper limit	0.93

Notes:

[36] - Based on a linear model with natural log-transformed IgG concentrations as response variable, and vaccination group and age category (2 months of age, ≥3 months of age) as factors. A conclusion of non-inferiority of V114 to PCV13 is based on the lower bound of the 2-sided 95% CI for the GMC ratio (V114/PVC 13) being >0.5 (1-sided p-value <0.025).

Secondary: GMC of Serotype-Specific IgG for the 2 Unique V114 Serotypes After Dose 3

End point title	GMC of Serotype-Specific IgG for the 2 Unique V114 Serotypes After Dose 3

End point description:

The anti-PnPs serotype-specific IgG GMCs of participants administered V114 versus participants administered PCV13 for the 2 unique V114 serotypes was determined using an electrochemiluminescence assay. All randomized participants without protocol deviations that could have substantially impacted the results of the immunogenicity endpoint and who had sufficient data to perform the analyses were analyzed. One participant in the PCV13 group did not receive PCV13 and therefore was not included in the analysis for this end point.

End point type	Secondary

End point timeframe:

30 days after Dose 3

End point values	V114	PCV13		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	347	346		
Units: µg/mL				
geometric mean (confidence interval 95%)				
Serotype 22F (Unique to V114) (n=339, 343)	6.59 (5.95 to 7.30)	0.06 (0.06 to 0.07)		
Serotype 33F (Unique to V114) (n=339, 337)	1.85 (1.60 to 2.14)	0.06 (0.05 to 0.07)		

Statistical analyses

Statistical analysis title	Serotype 33F

Statistical analysis description:

IgG GMC Ratio

Comparison groups	V114 v PCV13
Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	other[37]
Parameter estimate	GMC Ratio
Point estimate	32.48

Confidence interval	
level	95 %
sides	2-sided
lower limit	27.72
upper limit	38.05

Notes:

[37] - Based on a linear model with natural log-transformed IgG concentrations as response variable, and vaccination group and age category (2 months of age, ≥3 months of age) as factors.

Statistical analysis title	Serotype 22F

Statistical analysis description:

IgG GMC Ratio

Comparison groups	V114 v PCV13
Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	other[38]
Parameter estimate	GMC Ratio
Point estimate	107.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	96.18
upper limit	120.03

Notes:

[38] - Based on a linear model with natural log-transformed IgG concentrations as response variable, and vaccination group and age category (2 months of age, ≥3 months of age) as factors.

Secondary: Percentage of Participants Meeting the Serotype Specific IgG Threshold Value of ≥0.35 µg/mL for Each Serotype in V114 After Dose 4

End point title	Percentage of Participants Meeting the Serotype Specific IgG Threshold Value of ≥0.35 µg/mL for Each Serotype in V114 After Dose 4

End point description:

The anti-PnPs serotype-specific IgG response rates (percentage of participants meeting serotype-specific IgG threshold value of ≥0.35 µg/mL of participants administered V114 versus participants administered PCV13) for the 15 serotypes contained in V114 were determined using an electrochemiluminescence assay. All randomized participants without protocol deviations that could have substantially impacted the results of the immunogenicity endpoint and who had sufficient data to perform the analyses were analyzed. One participant in the PCV13 group did not receive PCV13 and therefore was not included in the analysis for this end point.

End point type	Secondary

End point timeframe:

30 Days after Dose 4

End point values	V114	PCV13		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	347	346		
Units: Percentage of Participants				
number (not applicable)				
Serotype 1 (Shared) (n=333, 334)	99.7	100.0		
Serotype 3 (Shared) (n=333, 334)	100.0	96.7		
Serotype 4 (Shared) (n=333, 334)	99.7	100.0		

Serotype 5 (Shared) (n=333, 334)	100.0	100.0		
Serotype 6A (Shared) (n=333, 334)	100.0	100.0		
Serotype 6B (Shared) (n=333, 334)	100.0	100.0		
Serotype 7F (Shared) (n=333, 334)	100.0	100.0		
Serotype 9V (Shared) (n=333, 334)	100.0	100.0		
Serotype 14 (Shared) (n=333, 334)	100.0	100.0		
Serotype 18C (Shared) (n=333, 334)	100.0	100.0		
Serotype 19A (Shared) (n=333, 334)	100.0	100.0		
Serotype 19F (Shared) (n=333, 334)	100.0	100.0		
Serotype 23F (Shared) (n=332, 334)	99.7	99.4		
Serotype 22F (Unique to V114) (n=333, 327)	100.0	5.2		
Serotype 33F (Unique to V114) (n=333, 313)	100.0	11.5		

Statistical analyses

Statistical analysis title	Serotype 1
Statistical analysis description:	
Participants With IgG ≥0.35 µg/mL	
Comparison groups	V114 v PCV13
Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	other[39]
Parameter estimate	Difference in Percent
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.7
upper limit	0.8

Notes:

[39] - The stratum-adjusted proportion difference using the Cochran-Mantel-Haenszel weight, and the corresponding 95% CI based on the method of Miettinen and Nurminen stratified by age category (2 months of age, ≥3 months of age).

Statistical analysis title	Serotype 3
Statistical analysis description:	
Participants With IgG ≥0.35 µg/mL	
Comparison groups	V114 v PCV13
Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	other[40]
Parameter estimate	Difference in Percent
Point estimate	3.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.8
upper limit	5.8

Notes:

[40] - The stratum-adjusted proportion difference using the Cochran-Mantel-Haenszel weight, and the corresponding 95% CI based on the method of Miettinen and Nurminen stratified by age category (2 months of age, ≥3 months of age).

Statistical analysis title	Serotype 4
Statistical analysis description:	
Participants With IgG ≥0.35 µg/mL	
Comparison groups	V114 v PCV13
Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	other[41]
Parameter estimate	Difference in Percent
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.7
upper limit	0.8

Notes:

[41] - The stratum-adjusted proportion difference using the Cochran-Mantel-Haenszel weight, and the corresponding 95% CI based on the method of Miettinen and Nurminen stratified by age category (2 months of age, ≥3 months of age).

Statistical analysis title	Serotype 5
Statistical analysis description:	
Participants With IgG ≥0.35 µg/mL	
Comparison groups	V114 v PCV13
Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	other[42]
Parameter estimate	Difference in Percent
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	1.1

Notes:

[42] - The stratum-adjusted proportion difference using the Cochran-Mantel-Haenszel weight, and the corresponding 95% CI based on the method of Miettinen and Nurminen stratified by age category (2 months of age, ≥3 months of age).

Statistical analysis title	Serotype 6A
Statistical analysis description:	
Participants With IgG ≥0.35 µg/mL	
Comparison groups	V114 v PCV13
Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	other[43]
Parameter estimate	Difference in Percent
Point estimate	0

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

Notes:

[43] - The stratum-adjusted proportion difference using the Cochran-Mantel-Haenszel weight, and the corresponding 95% CI based on the method of Miettinen and Nurminen stratified by age category (2 months of age, ≥3 months of age).

Statistical analysis title	Serotype 6B
Statistical analysis description:	
Participants With IgG ≥0.35 µg/mL	
Comparison groups	V114 v PCV13
Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	other[44]
Parameter estimate	Difference in Percent
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	1.1

Notes:

[44] - The stratum-adjusted proportion difference using the Cochran-Mantel-Haenszel weight, and the corresponding 95% CI based on the method of Miettinen and Nurminen stratified by age category (2 months of age, ≥3 months of age).

Statistical analysis title	Serotype 7F
Statistical analysis description:	
Participants With IgG ≥0.35 µg/mL	
Comparison groups	V114 v PCV13
Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	other[45]
Parameter estimate	Difference in Percent
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	1.1

Notes:

[45] - The stratum-adjusted proportion difference using the Cochran-Mantel-Haenszel weight, and the corresponding 95% CI based on the method of Miettinen and Nurminen stratified by age category (2 months of age, ≥3 months of age).

Statistical analysis title	Serotype 9V
Statistical analysis description:	
Participants With IgG ≥0.35 µg/mL	
Comparison groups	V114 v PCV13

Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	other[46]
Parameter estimate	Difference in Percent
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	1.1

Notes:

[46] - The stratum-adjusted proportion difference using the Cochran-Mantel-Haenszel weight, and the corresponding 95% CI based on the method of Miettinen and Nurminen stratified by age category (2 months of age, ≥3 months of age).

Statistical analysis title	Serotype 14
Statistical analysis description:	
Participants With IgG ≥0.35 µg/mL	
Comparison groups	V114 v PCV13
Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	other[47]
Parameter estimate	Difference in Percent
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	1.1

Notes:

[47] - The stratum-adjusted proportion difference using the Cochran-Mantel-Haenszel weight, and the corresponding 95% CI based on the method of Miettinen and Nurminen stratified by age category (2 months of age, ≥3 months of age).

Statistical analysis title	Serotype 18C
Statistical analysis description:	
Participants With IgG ≥0.35 µg/mL	
Comparison groups	V114 v PCV13
Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	other[48]
Parameter estimate	Difference in Percent
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	1.1

Notes:

[48] - The stratum-adjusted proportion difference using the Cochran-Mantel-Haenszel weight, and the corresponding 95% CI based on the method of Miettinen and Nurminen stratified by age category (2 months of age, ≥3 months of age).

Statistical analysis title	Serotype 19A

Statistical analysis description:	
Participants With IgG ≥0.35 µg/mL	
Comparison groups	V114 v PCV13
Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	other[49]
Parameter estimate	Difference in Percent
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	1.1

Notes:

[49] - The stratum-adjusted proportion difference using the Cochran-Mantel-Haenszel weight, and the corresponding 95% CI based on the method of Miettinen and Nurminen stratified by age category (2 months of age, ≥3 months of age).

Statistical analysis title	Serotype 19F
Statistical analysis description:	
Participants With IgG ≥0.35 µg/mL	
Comparison groups	V114 v PCV13
Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	other[50]
Parameter estimate	Difference in Percent
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	1.1

Notes:

[50] - The stratum-adjusted proportion difference using the Cochran-Mantel-Haenszel weight, and the corresponding 95% CI based on the method of Miettinen and Nurminen stratified by age category (2 months of age, ≥3 months of age).

Statistical analysis title	Serotype 23F
Statistical analysis description:	
Participants With IgG ≥0.35 µg/mL	
Comparison groups	V114 v PCV13
Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	other[51]
Parameter estimate	Difference in Percent
Point estimate	0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	1.9

Notes:

[51] - The stratum-adjusted proportion difference using the Cochran-Mantel-Haenszel weight, and the corresponding 95% CI based on the method of Miettinen and Nurminen stratified by age category (2 months of age, ≥3 months of age).

Statistical analysis title	Serotype 22F
Statistical analysis description:	
Participants With IgG ≥0.35 µg/mL	
Comparison groups	V114 v PCV13
Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	other[52]
Parameter estimate	Difference in Percent
Point estimate	94.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	91.8
upper limit	96.7

Notes:

[52] - The stratum-adjusted proportion difference using the Cochran-Mantel-Haenszel weight, and the corresponding 95% CI based on the method of Miettinen and Nurminen stratified by age category (2 months of age, ≥3 months of age).

Statistical analysis title	Serotype 33F
Statistical analysis description:	
Participants With IgG ≥0.35 µg/mL	
Comparison groups	V114 v PCV13
Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	other[53]
Parameter estimate	Difference in Percent
Point estimate	88.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	84.5
upper limit	91.6

Notes:

[53] - The stratum-adjusted proportion difference using the Cochran-Mantel-Haenszel weight, and the corresponding 95% CI based on the method of Miettinen and Nurminen stratified by age category (2 months of age, ≥3 months of age).

Secondary: GMC of Serotype-Specific IgG for Each Serotype in V114 After Dose 4

End point title	GMC of Serotype-Specific IgG for Each Serotype in V114 After Dose 4

End point description:

The anti-PnPs serotype-specific IgG GMCs of participants administered V114 versus participants administered PCV13 for the 15 serotypes contained in V114 was determined using an electrochemiluminescence assay. All randomized participants without protocol deviations that could have substantially impacted the results of the immunogenicity endpoint and who had sufficient data to perform the analyses were analyzed. One participant in the PCV13 group did not receive PCV13 and therefore was not included in the analysis for this end point.

End point type	Secondary

End point timeframe:

30 Days after Dose 4

End point values	V114	PCV13		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	347	346		
Units: µg/mL				
geometric mean (confidence interval 95%)				
Serotype 1 (Shared) (n=333, 334)	2.74 (2.47 to 3.04)	5.19 (4.68 to 5.77)		
Serotype 3 (Shared) (n=333, 334)	2.18 (1.97 to 2.41)	1.28 (1.15 to 1.41)		
Serotype 4 (Shared) (n=333, 334)	2.91 (2.57 to 3.30)	3.18 (2.81 to 3.59)		
Serotype 5 (Shared) (n=333, 334)	4.43 (3.96 to 4.95)	6.65 (5.95 to 7.43)		
Serotype 6A (Shared) (n=333, 334)	6.05 (5.36 to 6.81)	9.41 (8.35 to 10.60)		
Serotype 6B (Shared) (n=333, 334)	8.03 (7.12 to 9.05)	10.88 (9.66 to 12.26)		
Serotype 7F (Shared) (n=333, 334)	5.80 (5.15 to 6.54)	7.15 (6.35 to 8.05)		
Serotype 9V (Shared) (n=333, 334)	4.27 (3.79 to 4.81)	5.18 (4.60 to 5.83)		
Serotype 14 (Shared) (n=333, 334)	9.51 (8.45 to 10.69)	11.26 (10.02 to 12.66)		
Serotype 18C (Shared) (n=333, 334)	5.21 (4.60 to 5.89)	5.21 (4.61 to 5.90)		
Serotype 19A (Shared) (n=333, 334)	6.88 (6.20 to 7.63)	8.37 (7.55 to 9.28)		
Serotype 19F (Shared) (n=333, 334)	6.53 (5.89 to 7.22)	7.76 (7.01 to 8.58)		
Serotype 23F (Shared) (n=332, 334)	3.75 (3.26 to 4.31)	6.22 (5.42 to 7.15)		
Serotype 22F (Unique to V114) (n=333, 327)	11.42 (10.31 to 12.66)	0.13 (0.12 to 0.15)		
Serotype 33F (Unique to V114) (n=333, 313)	6.14 (5.48 to 6.89)	0.14 (0.12 to 0.15)		

Statistical analyses

Statistical analysis title	Serotype 1
Statistical analysis description: IgG GMC Ratio	
Comparison groups	V114 v PCV13
Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	other[54]
Parameter estimate	GMC Ratio
Point estimate	0.53

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.47
upper limit	0.59

Notes:

[54] - Based on a linear model with natural log-transformed IgG concentrations as response variable, and vaccination group and age category (2 months of age, ≥3 months of age) as factors.

Statistical analysis title	Serotype 3

Statistical analysis description:

IgG GMC Ratio

Comparison groups	V114 v PCV13
Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	other[55]
Parameter estimate	GMC Ratio
Point estimate	1.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.53
upper limit	1.9

Notes:

[55] - Based on a linear model with natural log-transformed IgG concentrations as response variable, and vaccination group and age category (2 months of age, ≥3 months of age) as factors.

Statistical analysis title	Serotype 4

Statistical analysis description:

IgG GMC Ratio

Comparison groups	V114 v PCV13
Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	other[56]
Parameter estimate	GMC Ratio
Point estimate	0.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8
upper limit	1.05

Notes:

[56] - Based on a linear model with natural log-transformed IgG concentrations as response variable, and vaccination group and age category (2 months of age, ≥3 months of age) as factors.

Statistical analysis title	Serotype 5

Statistical analysis description:

IgG GMC Ratio

Comparison groups	V114 v PCV13

Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	other[57]
Parameter estimate	GMC Ratio
Point estimate	0.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.59
upper limit	0.75

Notes:

[57] - Based on a linear model with natural log-transformed IgG concentrations as response variable, and vaccination group and age category (2 months of age, ≥3 months of age) as factors.

Statistical analysis title	Serotype 6A

Statistical analysis description:

IgG GMC Ratio

Comparison groups	V114 v PCV13
Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	other[58]
Parameter estimate	GMC Ratio
Point estimate	0.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.56
upper limit	0.73

Notes:

[58] - Based on a linear model with natural log-transformed IgG concentrations as response variable, and vaccination group and age category (2 months of age, ≥3 months of age) as factors.

Statistical analysis title	Serotype 6B

Statistical analysis description:

IgG GMC Ratio

Comparison groups	V114 v PCV13
Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	other[59]
Parameter estimate	GMC Ratio
Point estimate	0.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.65
upper limit	0.84

Notes:

[59] - Based on a linear model with natural log-transformed IgG concentrations as response variable, and vaccination group and age category (2 months of age, ≥3 months of age) as factors.

Statistical analysis title	Serotype 7F

Statistical analysis description:

IgG GMC Ratio

Comparison groups	V114 v PCV13
Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	other[60]
Parameter estimate	GMC Ratio
Point estimate	0.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	0.92

Notes:

[60] - Based on a linear model with natural log-transformed IgG concentrations as response variable, and vaccination group and age category (2 months of age, ≥3 months of age) as factors.

Statistical analysis title	Serotype 9V
Statistical analysis description:	
IgG GMC Ratio	
Comparison groups	V114 v PCV13
Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	other[61]
Parameter estimate	GMC Ratio
Point estimate	0.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.73
upper limit	0.94

Notes:

[61] - Based on a linear model with natural log-transformed IgG concentrations as response variable, and vaccination group and age category (2 months of age, ≥3 months of age) as factors.

Statistical analysis title	Serotype 14
Statistical analysis description:	
IgG GMC Ratio	
Comparison groups	V114 v PCV13
Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	other[62]
Parameter estimate	GMC Ratio
Point estimate	0.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.74
upper limit	0.96

Notes:

[62] - Based on a linear model with natural log-transformed IgG concentrations as response variable, and vaccination group and age category (2 months of age, ≥3 months of age) as factors.

Statistical analysis title	Serotype 18C

Statistical analysis description:	
IgG GMC Ratio	
Comparison groups	V114 v PCV13
Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	other[63]
Parameter estimate	GMC Ratio
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.87
upper limit	1.14

Notes:

[63] - Based on a linear model with natural log-transformed IgG concentrations as response variable, and vaccination group and age category (2 months of age, ≥3 months of age) as factors.

Statistical analysis title	Serotype 19A
Statistical analysis description:	
IgG GMC Ratio	
Comparison groups	V114 v PCV13
Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	other[64]
Parameter estimate	GMC Ratio
Point estimate	0.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.73
upper limit	0.92

Notes:

[64] - Based on a linear model with natural log-transformed IgG concentrations as response variable, and vaccination group and age category (2 months of age, ≥3 months of age) as factors.

Statistical analysis title	Serotype 19F
Statistical analysis description:	
IgG GMC Ratio	
Comparison groups	V114 v PCV13
Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	other[65]
Parameter estimate	GMC Ratio
Point estimate	0.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.75
upper limit	0.94

Notes:

[65] - Based on a linear model with natural log-transformed IgG concentrations as response variable, and vaccination group and age category (2 months of age, ≥3 months of age) as factors.

Statistical analysis title	Serotype 23F
Statistical analysis description:	
IgG GMC Ratio	
Comparison groups	V114 v PCV13
Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	other[66]
Parameter estimate	GMC Ratio
Point estimate	0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.52
upper limit	0.7

Notes:

[66] - Based on a linear model with natural log-transformed IgG concentrations as response variable, and vaccination group and age category (2 months of age, ≥3 months of age) as factors.

Statistical analysis title	Serotype 22F
Statistical analysis description:	
IgG GMC Ratio	
Comparison groups	V114 v PCV13
Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	other[67]
Parameter estimate	GMC Ratio
Point estimate	86.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	77.61
upper limit	96.95

Notes:

[67] - Based on a linear model with natural log-transformed IgG concentrations as response variable, and vaccination group and age category (2 months of age, ≥3 months of age) as factors.

Statistical analysis title	Serotype 33F
Statistical analysis description:	
IgG GMC Ratio	
Comparison groups	V114 v PCV13
Number of subjects included in analysis	693
Analysis specification	Pre-specified
Analysis type	other[68]
Parameter estimate	GMC Ratio
Point estimate	45.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	40.07
upper limit	51.54

Notes:

[68] - Based on a linear model with natural log-transformed IgG concentrations as response variable, and vaccination group and age category (2 months of age, ≥3 months of age) as factors.

Secondary: Geometric Mean Titer of Serotype-Specific Opsonophagocytic Activity for Each Serotype in V114 After Dose 3

End point title	Geometric Mean Titer of Serotype-Specific Opsonophagocytic Activity for Each Serotype in V114 After Dose 3

End point description:

The anti-PnPs serotype-specific opsonophagocytic activity (OPA) and geometric mean titers (GMTs) of participants administered V114 versus participants administered PCV13 for the 15 serotypes contained in V114 was determined using a multiplexed opsonophagocytic assay. All randomized participants without protocol deviations that could have substantially impacted the results of the immunogenicity endpoint and who had sufficient data to perform the analyses were analyzed. One participant in the PCV13 group did not receive PCV13 and therefore was not included in the analysis for this end point.

End point type	Secondary

End point timeframe:

30 Days after Dose 3

End point values	V114	PCV13		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	343	346		
Units: Titer				
geometric mean (confidence interval 95%)				
Serotype 1 (Shared) (n=336, 340)	211.51 (180.48 to 247.86)	322.44 (275.23 to 377.76)		
Serotype 3 (Shared) (n=333, 336)	660.68 (586.60 to 744.11)	471.43 (418.48 to 531.08)		
Serotype 4 (Shared) (n=334, 338)	3984.87 (3537.66 to 4488.62)	4118.16 (3656.82 to 4637.70)		
Serotype 5 (Shared) (n=336, 339)	1241.69 (1098.82 to 1403.14)	1358.43 (1202.35 to 1534.79)		
Serotype 6A (Shared) (n=334, 336)	9124.96 (7894.53 to 10547.16)	11956.64 (10340.85 to 13824.91)		
Serotype 6B (Shared) (n=334, 338)	8416.19 (7243.92 to 9778.18)	10421.94 (8972.87 to 12105.02)		
Serotype 7F (Shared) (n=334, 338)	22324.41 (19365.68 to 25735.19)	27396.28 (23771.84 to 31573.33)		
Serotype 9V (Shared) (n=334, 338)	2725.29 (2399.27 to 3095.62)	3338.40 (2939.75 to 3791.11)		
Serotype 14 (Shared) (n=334, 339)	14175.13 (12024.73 to 16710.08)	12288.35 (10433.90 to 14472.40)		
Serotype 18C (Shared) (n=334, 339)	3698.24 (3346.73 to 4086.66)	3705.21 (3353.84 to 4093.39)		
Serotype 19A (Shared) (n=335, 339)	2709.90 (2418.02 to 3037.02)	3961.10 (3535.23 to 4438.26)		

Serotype 19F (Shared) (n=334, 339)	2371.39 (2141.38 to 2624.87)	2541.27 (2297.18 to 2811.29)		
Serotype 23F (Shared) (n=334, 340)	11861.63 (10118.30 to 13905.32)	18957.26 (16186.86 to 22201.82)		
Serotype 22F (Unique to V114) (n=333, 333)	5575.08 (4769.68 to 6516.47)	9.95 (8.51 to 11.63)		
Serotype 33F (Unique to V114) (n=333, 334)	23888.79 (17632.59 to 32364.75)	121.79 (89.73 to 165.32)		

Statistical analyses

Statistical analysis title	Serotype 1
Statistical analysis description:	
OPA GMT Ratio	
Comparison groups	V114 v PCV13
Number of subjects included in analysis	689
Analysis specification	Pre-specified
Analysis type	other[69]
Parameter estimate	GMT Ratio
Point estimate	0.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.55
upper limit	0.78

Notes:

[69] - Based on a linear model with natural log-transformed OPA titers as response variable, and vaccination group and age
category (2 months of age, ≥3 months of age) as factors.

Statistical analysis title	Serotype 3
Statistical analysis description:	
OPA GMT Ratio	
Comparison groups	V114 v PCV13
Number of subjects included in analysis	689
Analysis specification	Pre-specified
Analysis type	other[70]
Parameter estimate	GMT Ratio
Point estimate	1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.23
upper limit	1.59

Notes:

[70] - Based on a linear model with natural log-transformed OPA titers as response variable, and vaccination group and age
category (2 months of age, ≥3 months of age) as factors.

Statistical analysis title	Serotype 4
Statistical analysis description:	
OPA GMT Ratio	
Comparison groups	V114 v PCV13
Number of subjects included in analysis	689
Analysis specification	Pre-specified
Analysis type	other[71]
Parameter estimate	GMT Ratio
Point estimate	0.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.85
upper limit	1.1

Notes:

[71] - Based on a linear model with natural log-transformed OPA titers as response variable, and vaccination group and age
category (2 months of age, ≥3 months of age) as factors.

Statistical analysis title	Serotype 5
Statistical analysis description:	
OPA GMT Ratio	
Comparison groups	V114 v PCV13
Number of subjects included in analysis	689
Analysis specification	Pre-specified
Analysis type	other[72]
Parameter estimate	GMT Ratio
Point estimate	0.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8
upper limit	1.04

Notes:

[72] - Based on a linear model with natural log-transformed OPA titers as response variable, and vaccination group and age
category (2 months of age, ≥3 months of age) as factors.

Statistical analysis title	Serotype 6A
Statistical analysis description:	
OPA GMT Ratio	
Comparison groups	V114 v PCV13
Number of subjects included in analysis	689
Analysis specification	Pre-specified
Analysis type	other[73]
Parameter estimate	GMT Ratio
Point estimate	0.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.65
upper limit	0.89

Notes:

[73] - Based on a linear model with natural log-transformed OPA titers as response variable, and vaccination group and age
category (2 months of age, ≥3 months of age) as factors.

Statistical analysis title	Serotype 6B
Statistical analysis description:	
OPA GMT Ratio	
Comparison groups	V114 v PCV13
Number of subjects included in analysis	689
Analysis specification	Pre-specified
Analysis type	other[74]
Parameter estimate	GMC Ratio
Point estimate	0.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.69
upper limit	0.95

Notes:

[74] - Based on a linear model with natural log-transformed OPA titers as response variable, and vaccination group and age
category (2 months of age, ≥3 months of age) as factors.

Statistical analysis title	Serotype 7F
Statistical analysis description:	
OPA GMT Ratio	
Comparison groups	V114 v PCV13
Number of subjects included in analysis	689
Analysis specification	Pre-specified
Analysis type	other[75]
Parameter estimate	GMC Ratio
Point estimate	0.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	0.95

Notes:

[75] - Based on a linear model with natural log-transformed OPA titers as response variable, and vaccination group and age
category (2 months of age, ≥3 months of age) as factors.

Statistical analysis title	Serotype 9V
Statistical analysis description:	
OPA GMT Ratio	
Comparison groups	V114 v PCV13
Number of subjects included in analysis	689
Analysis specification	Pre-specified
Analysis type	other[76]
Parameter estimate	GMT Ratio
Point estimate	0.82

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	0.94

Notes:

[76] - Based on a linear model with natural log-transformed OPA titers as response variable, and vaccination group and age
category (2 months of age, ≥3 months of age) as factors.

Statistical analysis title	Serotype 14

Statistical analysis description:

OPA GMT Ratio

Comparison groups	V114 v PCV13
Number of subjects included in analysis	689
Analysis specification	Pre-specified
Analysis type	other[77]
Parameter estimate	GMT Ratio
Point estimate	1.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.97
upper limit	1.38

Notes:

[77] - Based on a linear model with natural log-transformed OPA titers as response variable, and vaccination group and age
category (2 months of age, ≥3 months of age) as factors.

Statistical analysis title	Serotype 18C

Statistical analysis description:

OPA GMT Ratio

Comparison groups	V114 v PCV13
Number of subjects included in analysis	689
Analysis specification	Pre-specified
Analysis type	other[78]
Parameter estimate	GMT Ratio
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.9
upper limit	1.11

Notes:

[78] - Based on a linear model with natural log-transformed OPA titers as response variable, and vaccination group and age
category (2 months of age, ≥3 months of age) as factors.

Statistical analysis title	Serotype 19A

Statistical analysis description:

OPA GMT Ratio

Comparison groups	V114 v PCV13

Number of subjects included in analysis	689
Analysis specification	Pre-specified
Analysis type	other[79]
Parameter estimate	GMT Ratio
Point estimate	0.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.61
upper limit	0.77

Notes:

[79] - Based on a linear model with natural log-transformed OPA titers as response variable, and vaccination group and age
category (2 months of age, ≥3 months of age) as factors.

Statistical analysis title	Serotype 19F

Statistical analysis description:

OPA GMT Ratio

Comparison groups	V114 v PCV13
Number of subjects included in analysis	689
Analysis specification	Pre-specified
Analysis type	other[80]
Parameter estimate	GMT Ratio
Point estimate	0.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.84
upper limit	1.04

Notes:

[80] - Based on a linear model with natural log-transformed OPA titers as response variable, and vaccination group and age
category (2 months of age, ≥3 months of age) as factors.

Statistical analysis title	Serotype 23F

Statistical analysis description:

OPA GMT Ratio

Comparison groups	V114 v PCV13
Number of subjects included in analysis	689
Analysis specification	Pre-specified
Analysis type	other[81]
Parameter estimate	GMT Ratio
Point estimate	0.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.53
upper limit	0.74

Notes:

[81] - Based on a linear model with natural log-transformed OPA titers as response variable, and vaccination group and age
category (2 months of age, ≥3 months of age) as factors.

Statistical analysis title	Serotype 22F

Statistical analysis description:

OPA GMT Ratio

Comparison groups	V114 v PCV13
Number of subjects included in analysis	689
Analysis specification	Pre-specified
Analysis type	other[82]
Parameter estimate	GMT Ratio
Point estimate	560.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	474.05
upper limit	662.63

Notes:

[82] - Based on a linear model with natural log-transformed OPA titers as response variable, and vaccination group and age
category (2 months of age, ≥3 months of age) as factors.

Statistical analysis title	Serotype 33F

Statistical analysis description:

OPA GMT Ratio

Comparison groups	V114 v PCV13
Number of subjects included in analysis	689
Analysis specification	Pre-specified
Analysis type	other[83]
Parameter estimate	GMT Ratio
Point estimate	196.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	141.85
upper limit	271.21

Notes:

[83] - Based on a linear model with natural log-transformed OPA titers as response variable, and vaccination group and age
category (2 months of age, ≥3 months of age) as factors.

Secondary: GMT of Serotype-Specific OPA for Each Serotype in V114 After Dose 4

End point title	GMT of Serotype-Specific OPA for Each Serotype in V114 After Dose 4

End point description:

The anti-PnPs serotype-specific opsonophagocytic activity (OPA) and geometric mean titers (GMTs) of participants administered V114 versus participants administered PCV13 for the 15 serotypes contained in V114 was determined using a multiplexed opsonophagocytic assay. The first 50% of all participants with sufficient serum volume after dose 3 to evaluate OPA responses were analyzed. One participant in the PCV13 group did not receive PCV13 and therefore was not included in the analysis for this end point.

End point type	Secondary

End point timeframe:

30 Days after Dose 4

End point values	V114	PCV13		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	343	346		
Units: Titer				
geometric mean (confidence interval 95%)				
Serotype 1 (Shared) (n=156, 156)	453.42 (327.21 to 628.32)	854.50 (616.64 to 1184.10)		
Serotype 3 (Shared) (n=150, 146)	1444.00 (1166.36 to 1787.72)	893.97 (720.25 to 1109.58)		
Serotype 4 (Shared) (n=153, 152)	4531.52 (3592.99 to 5715.21)	6264.94 (4957.63 to 7916.97)		
Serotype 5 (Shared) (n=157, 154)	1853.08 (1439.01 to 2386.30)	2151.95 (1669.81 to 2773.30)		
Serotype 6A (Shared) (n=152, 152)	12553.06 (10072.11 to 15645.13)	17476.24 (13999.28 to 21816.75)		
Serotype 6B (Shared) (n=153, 153)	9218.64 (7346.96 to 11567.14)	14041.53 (11171.79 to 17648.42)		
Serotype 7F (Shared) (n=155, 155)	15451.96 (12500.49 to 19100.31)	18039.04 (14593.41 to 22298.22)		
Serotype 9V (Shared) (n=152, 154)	3259.24 (2548.05 to 4168.93)	5050.89 (3957.89 to 6445.73)		
Serotype 14 (Shared) (n=154, 155)	8486.72 (6720.27 to 10717.49)	5719.04 (4521.91 to 7233.08)		
Serotype 18C (Shared) (n=153, 153)	7027.62 (5704.70 to 8657.32)	5903.86 (4785.06 to 7284.24)		
Serotype 19A (Shared) (n=155, 156)	8441.43 (6620.55 to 10763.11)	10834.58 (8499.57 to 13811.07)		
Serotype 19F (Shared) (n=153, 156)	4716.70 (3863.66 to 5758.07)	3829.62 (3138.93 to 4672.28)		
Serotype 23F (Shared) (n=153, 153)	11319.82 (8635.69 to 14838.22)	30686.58 (23314.40 to 40389.89)		
Serotype 22F (Unique to V114) (n=156, 144)	5561.71 (3730.30 to 8292.26)	35.68 (23.67 to 53.79)		
Serotype 33F (Unique to V114) (n=154, 152)	19899.34 (14204.44 to 27877.46)	1183.52 (844.22 to 1659.18)		

Statistical analyses

Statistical analysis title	Serotype 1
Statistical analysis description: OPA GMT Ratio	
Comparison groups	V114 v PCV13

Number of subjects included in analysis	689
Analysis specification	Pre-specified
Analysis type	other[84]
Parameter estimate	GMT Ratio
Point estimate	0.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.38
upper limit	0.75

Notes:

[84] - Based on a linear model with natural log-transformed OPA titers as response variable, and vaccination group and age
category (2 months of age, ≥3 months of age) as factors.

Statistical analysis title	Serotype 3

Statistical analysis description:

OPA GMT Ratio

Comparison groups	V114 v PCV13
Number of subjects included in analysis	689
Analysis specification	Pre-specified
Analysis type	other[85]
Parameter estimate	GMT Ratio
Point estimate	1.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.28
upper limit	2.03

Notes:

[85] - Based on a linear model with natural log-transformed OPA titers as response variable, and vaccination group and age
category (2 months of age, ≥3 months of age) as factors.

Statistical analysis title	Serotype 4

Statistical analysis description:

OPA GMT Ratio

Comparison groups	V114 v PCV13
Number of subjects included in analysis	689
Analysis specification	Pre-specified
Analysis type	other[86]
Parameter estimate	GMT Ratio
Point estimate	0.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.57
upper limit	0.93

Notes:

[86] - Based on a linear model with natural log-transformed OPA titers as response variable, and vaccination group and age
category (2 months of age, ≥3 months of age) as factors.

Statistical analysis title	Serotype 5

Statistical analysis description:	
OPA GMT Ratio	
Comparison groups	V114 v PCV13
Number of subjects included in analysis	689
Analysis specification	Pre-specified
Analysis type	other[87]
Parameter estimate	GMT Ratio
Point estimate	0.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.66
upper limit	1.13

Notes:

[87] - Based on a linear model with natural log-transformed OPA titers as response variable, and vaccination group and age
category (2 months of age, ≥3 months of age) as factors.

Statistical analysis title	Serotype 6A
Statistical analysis description:	
OPA GMT Ratio	
Comparison groups	V114 v PCV13
Number of subjects included in analysis	689
Analysis specification	Pre-specified
Analysis type	other[88]
Parameter estimate	GMT Ratio
Point estimate	0.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.57
upper limit	0.91

Notes:

[88] - Based on a linear model with natural log-transformed OPA titers as response variable, and vaccination group and age
category (2 months of age, ≥3 months of age) as factors.

Statistical analysis title	Serotype 6B
Statistical analysis description:	
OPA GMT Ratio	
Comparison groups	V114 v PCV13
Number of subjects included in analysis	689
Analysis specification	Pre-specified
Analysis type	other[89]
Parameter estimate	GMT Ratio
Point estimate	0.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.52
upper limit	0.83

Notes:

[89] - Based on a linear model with natural log-transformed OPA titers as response variable, and vaccination group and age
category (2 months of age, ≥3 months of age) as factors.

Statistical analysis title	Serotype 7F
Statistical analysis description:	
OPA GMT Ratio	
Comparison groups	V114 v PCV13
Number of subjects included in analysis	689
Analysis specification	Pre-specified
Analysis type	other[90]
Parameter estimate	GMT Ratio
Point estimate	0.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.68
upper limit	1.07

Notes:

[90] - Based on a linear model with natural log-transformed OPA titers as response variable, and vaccination group and age
category (2 months of age, ≥3 months of age) as factors.

Statistical analysis title	Serotype 9V
Statistical analysis description:	
OPA GMT Ratio	
Comparison groups	V114 v PCV13
Number of subjects included in analysis	689
Analysis specification	Pre-specified
Analysis type	other[91]
Parameter estimate	GMT Ratio
Point estimate	0.65
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5
upper limit	0.84

Notes:

[91] - Based on a linear model with natural log-transformed OPA titers as response variable, and vaccination group and age
category (2 months of age, ≥3 months of age) as factors.

Statistical analysis title	Serotype 14
Statistical analysis description:	
OPA GMT Ratio	
Comparison groups	V114 v PCV13
Number of subjects included in analysis	689
Analysis specification	Pre-specified
Analysis type	other[92]
Parameter estimate	GMT Ratio
Point estimate	1.48

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.16
upper limit	1.9

Notes:

[92] - Based on a linear model with natural log-transformed OPA titers as response variable, and vaccination group and age
category (2 months of age, ≥3 months of age) as factors.

Statistical analysis title	Serotype 18C

Statistical analysis description:

OPA GMT Ratio

Comparison groups	V114 v PCV13
Number of subjects included in analysis	689
Analysis specification	Pre-specified
Analysis type	other[93]
Parameter estimate	GMT Ratio
Point estimate	1.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.95
upper limit	1.48

Notes:

[93] - Based on a linear model with natural log-transformed OPA titers as response variable, and vaccination group and age
category (2 months of age, ≥3 months of age) as factors.

Statistical analysis title	Serotype 19A

Statistical analysis description:

OPA GMT Ratio

Comparison groups	V114 v PCV13
Number of subjects included in analysis	689
Analysis specification	Pre-specified
Analysis type	other[94]
Parameter estimate	GMT Ratio
Point estimate	0.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	1.01

Notes:

[94] - Based on a linear model with natural log-transformed OPA titers as response variable, and vaccination group and age
category (2 months of age, ≥3 months of age) as factors.

Statistical analysis title	Serotype 19F

Statistical analysis description:

OPA GMT Ratio

Comparison groups	V114 v PCV13

Number of subjects included in analysis	689
Analysis specification	Pre-specified
Analysis type	other[95]
Parameter estimate	GMT Ratio
Point estimate	1.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	1
upper limit	1.52

Notes:

[95] - Based on a linear model with natural log-transformed OPA titers as response variable, and vaccination group and age
category (2 months of age, ≥3 months of age) as factors.

Statistical analysis title	Serotype 23F

Statistical analysis description:

OPA GMT Ratio

Comparison groups	V114 v PCV13
Number of subjects included in analysis	689
Analysis specification	Pre-specified
Analysis type	other[96]
Parameter estimate	GMT Ratio
Point estimate	0.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.28
upper limit	0.49

Notes:

[96] - Based on a linear model with natural log-transformed OPA titers as response variable, and vaccination group and age
category (2 months of age, ≥3 months of age) as factors.

Statistical analysis title	Serotype 22F

Statistical analysis description:

OPA GMT Ratio

Comparison groups	V114 v PCV13
Number of subjects included in analysis	689
Analysis specification	Pre-specified
Analysis type	other[97]
Parameter estimate	GMT Ratio
Point estimate	155.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	101.84
upper limit	238.59

Notes:

[97] - Based on a linear model with natural log-transformed OPA titers as response variable, and vaccination group and age
category (2 months of age, ≥3 months of age) as factors.

Statistical analysis title	Serotype 33F

Statistical analysis description:	
OPA GMT Ratio	
Comparison groups	V114 v PCV13
Number of subjects included in analysis	689
Analysis specification	Pre-specified
Analysis type	other[98]
Parameter estimate	GMT Ratio
Point estimate	16.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	11.74
upper limit	24.08

Notes:

[98] - Based on a linear model with natural log-transformed OPA titers as response variable, and vaccination group and age
category (2 months of age, ≥3 months of age) as factors.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Non-serious adverse events: Up to 14 days after each vaccination; Serious adverse events: Approximately 1 month after Dose 4 (Up to 14 months); All-cause mortality: Up to 17 months

Adverse event reporting additional description:

The analysis population for deaths (all-causes) included all randomized participants (N=347, N=347). The analysis population for AEs included all randomized participants who received at least 1 dose of study vaccination. One participant in the PCV13 group did not receive PCV13.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups

Reporting group title	V114

Reporting group description: -

Reporting group title	PCV13

Reporting group description: -

Serious adverse events	V114	PCV13	
Total subjects affected by serious adverse events			
subjects affected / exposed	24 / 347 (6.92%)	23 / 346 (6.65%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Congenital, familial and genetic disorders			
Hamartoma			
subjects affected / exposed	1 / 347 (0.29%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Kawasaki's disease			
subjects affected / exposed	1 / 347 (0.29%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Febrile convulsion			
subjects affected / exposed	1 / 347 (0.29%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Seizure			
subjects affected / exposed	1 / 347 (0.29%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 347 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 347 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Food allergy			
subjects affected / exposed	3 / 347 (0.86%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Milk allergy			
subjects affected / exposed	1 / 347 (0.29%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Intussusception			
subjects affected / exposed	0 / 347 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 347 (0.00%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract inflammation			

subjects affected / exposed	0 / 347 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Compartment syndrome			
subjects affected / exposed	0 / 347 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Adenovirus infection			
subjects affected / exposed	1 / 347 (0.29%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial infection			
subjects affected / exposed	1 / 347 (0.29%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchiolitis			
subjects affected / exposed	0 / 347 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	1 / 347 (0.29%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	1 / 347 (0.29%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia urinary tract infection			
subjects affected / exposed	1 / 347 (0.29%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Gastroenteritis norovirus			
subjects affected / exposed	1 / 347 (0.29%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	1 / 347 (0.29%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphadenitis bacterial			
subjects affected / exposed	0 / 347 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephritis bacterial			
subjects affected / exposed	1 / 347 (0.29%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	3 / 347 (0.86%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia bacterial			
subjects affected / exposed	0 / 347 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia respiratory syncytial viral			
subjects affected / exposed	0 / 347 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus bronchiolitis			
subjects affected / exposed	0 / 347 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia viral			

subjects affected / exposed	0 / 347 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus infection			
subjects affected / exposed	4 / 347 (1.15%)	3 / 346 (0.87%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus bronchitis			
subjects affected / exposed	1 / 347 (0.29%)	2 / 346 (0.58%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	4 / 347 (1.15%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			
subjects affected / exposed	1 / 347 (0.29%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral pharyngitis			
subjects affected / exposed	1 / 347 (0.29%)	0 / 346 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral rash			
subjects affected / exposed	0 / 347 (0.00%)	1 / 346 (0.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	V114	PCV13	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	340 / 347 (97.98%)	340 / 346 (98.27%)	
Nervous system disorders			
Somnolence			
subjects affected / exposed	194 / 347 (55.91%)	190 / 346 (54.91%)	
occurrences (all)	430	399	
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	306 / 347 (88.18%)	309 / 346 (89.31%)	
occurrences (all)	878	929	
Injection site induration			
subjects affected / exposed	281 / 347 (80.98%)	281 / 346 (81.21%)	
occurrences (all)	813	787	
Injection site pain			
subjects affected / exposed	108 / 347 (31.12%)	83 / 346 (23.99%)	
occurrences (all)	178	134	
Injection site swelling			
subjects affected / exposed	263 / 347 (75.79%)	276 / 346 (79.77%)	
occurrences (all)	670	688	
Pyrexia			
subjects affected / exposed	227 / 347 (65.42%)	252 / 346 (72.83%)	
occurrences (all)	544	610	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	35 / 347 (10.09%)	20 / 346 (5.78%)	
occurrences (all)	43	22	
Respiratory, thoracic and mediastinal disorders			
Rhinorrhoea			
subjects affected / exposed	10 / 347 (2.88%)	21 / 346 (6.07%)	
occurrences (all)	12	23	
Skin and subcutaneous tissue disorders			
Eczema infantile			
subjects affected / exposed	18 / 347 (5.19%)	16 / 346 (4.62%)	
occurrences (all)	19	16	
Erythema			

subjects affected / exposed	33 / 347 (9.51%)	31 / 346 (8.96%)	
occurrences (all)	44	42	
Rash			
subjects affected / exposed	17 / 347 (4.90%)	18 / 346 (5.20%)	
occurrences (all)	21	22	
Skin induration			
subjects affected / exposed	23 / 347 (6.63%)	18 / 346 (5.20%)	
occurrences (all)	29	22	
Psychiatric disorders			
Irritability			
subjects affected / exposed	231 / 347 (66.57%)	210 / 346 (60.69%)	
occurrences (all)	522	500	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	32 / 347 (9.22%)	37 / 346 (10.69%)	
occurrences (all)	34	39	
Upper respiratory tract infection			
subjects affected / exposed	20 / 347 (5.76%)	22 / 346 (6.36%)	
occurrences (all)	23	29	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	83 / 347 (23.92%)	84 / 346 (24.28%)	
occurrences (all)	132	117	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 August 2020	Amendment 01: Primary reason for amendment was to change the primary objectives for the evaluation of this study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported