Clinical trial results:
A Phase 3, Multicenter, Randomized, Double-blind, Active-comparator-controlled Study to Evaluate the Safety, Tolerability, and Immunogenicity of a 3-dose Regimen of V114 in Healthy Infants (PNEU-PED-EU-2)

Summary

EudraCT number	2018-003788-70
Trial protocol	FI NO DK SE IT
Global end of trial date	02 November 2021

Results information

Result version number	v2 (current)
This version publication date	29 December 2022
First version publication date	13 May 2022
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	V114-026

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04016714
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Merck Sharp & Dohme Corp.
Sponsor organisation address	2000 Galloping Hill Road, Kenilworth, NJ, United States, 07033
Public contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., 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	29 October 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 October 2021
Global end of trial reached?	Yes
Global end of trial date	02 November 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study was to evaluate the safety, tolerability, and immunogenicity of a 3-dose schedule (2-dose primary series followed by a toddler dose) of pneumococcal conjugate vaccine (PCV) as one of the currently recommended by the World Health Organization (WHO) Strategic Advisory Group of Experts (SAGE) on Immunizations and practiced in many countries. The primary hypotheses were: V114 is non-inferior to Prevenar 13™ for the 13 shared serotypes based on response rates and on anti-pneumococcal polysaccharide (PnPs) serotype-specific Immunoglobulin G (IgG) geometric mean concentrations (GMCs) 30 days after Dose 3; V114 is superior to Prevenar 13™ for the 2 serotypes unique to V114 based on the response rates and on anti-PnPs serotype-specific IgG GMCs 30 days after Dose 3; and Vaxelis™ administered concomitantly with V114 is non-inferior to Vaxelis™ administered concomitantly with Prevenar 13™ 30 days after Dose 3 for each antigen included in Vaxelis™.

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	28 August 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Denmark: 379
Country: Number of subjects enrolled	Finland: 612
Country: Number of subjects enrolled	Italy: 105
Country: Number of subjects enrolled	Norway: 95
Worldwide total number of subjects	1191
EEA total number of subjects	1191

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)	1191
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

This study enrolled healthy infants. Other inclusion criteria applied.

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, Carer, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	V114

Arm description:

Participants received a single 0.5 mL intramuscular (IM) injection of V114 at Visit 1, 2, and 4 (approximately 3, 5, and 12 months of age). As part of the study design, participants also received other pediatric vaccines, including Vaxelis™ (0.5 mL single dose at Visits 1, 2, and 4); M-M-R™II (0.5 mL single dose at Visit 4); and VARIVAX™ (0.5 mL single dose at Visit 4, except participants in Norway and Denmark, who received a second dose of VARIVAX™ at Visit 5, according to local vaccination requirements).

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

Dosage and administration details:

15-valent pneumococcal conjugate vaccine with serotypes 1, 3, 4, 5, 6A, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F, 33F, serotype 6B and aluminum phosphate adjuvant in each 0.5 mL dose.

Investigational medicinal product name	Vaxelis™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL single dose

Investigational medicinal product name	M-M-R™II
Investigational medicinal product code	
Other name	Measles, Mumps, and Rubella Virus Vaccine Live
Pharmaceutical forms	Suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

0.5 mL single dose

Investigational medicinal product name	Varivax™
Investigational medicinal product code	
Other name	Varicella Vaccine Live
Pharmaceutical forms	Suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

0.5 mL single dose

Arm title	Prevenar 13™

Arm description:

Participants received a single 0.5 mL IM injection of Prevenar 13™ at Visit 1, 2, and 4 (approximately 3, 5, and 12 months of age). As part of the study design, participants also received other pediatric vaccines, including Vaxelis™ (0.5 mL single dose at Visits 1, 2, and 4); M-M-R™II (0.5 mL single dose at Visit 4); and VARIVAX™ (0.5 mL single dose at Visit 4, except participants in Norway and Denmark, who received a second dose of VARIVAX™ at Visit 5, according to local vaccination requirements).

Arm type	Active comparator
Investigational medicinal product name	Prevenar 13™
Investigational medicinal product code	
Other name	Pneumococcal 13-valent Conjugate Vaccine
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

13-valent pneumococcal capsular polysaccharide with serotypes 1, 3, 4, 5, 6A, 7F, 9V, 14, 18C, 19A, 19F, 23F (2.2 mcg) and 6B (4.4 mcg) in each 0.5 ml dose

Investigational medicinal product name	Varivax™
Investigational medicinal product code	
Other name	Varicella Vaccine Live
Pharmaceutical forms	Suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

0.5 mL single dose

Investigational medicinal product name	M-M-R™II
Investigational medicinal product code	
Other name	Measles, Mumps, and Rubella Virus Vaccine Live
Pharmaceutical forms	Suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

0.5 mL single dose

Investigational medicinal product name	Vaxelis™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL single dose

Number of subjects in period 1	V114	Prevenar 13™
Started	595	596
Vaccination 1 (V114 or Prevenar 13™)	595	596
Vaccination 2 (V114 or Prevenar 13™)	585	588
Vaccination 3 (V114 or Prevenar 13™)	573	581

Completed	572	580
Not completed	23	16
Physician decision	3	3
Death	1	-
Withdrawal by Parent/Guardian	16	12
Lost to follow-up	3	1

Baseline characteristics

Reporting groups	
Reporting group title	V114
Reporting group description:	
Participants received a single 0.5 mL intramuscular (IM) injection of V114 at Visit 1, 2, and 4 (approximately 3, 5, and 12 months of age). As part of the study design, participants also received other pediatric vaccines, including Vaxelis™ (0.5 mL single dose at Visits 1, 2, and 4); M-M-R™II (0.5 mL single dose at Visit 4); and VARIVAX™ (0.5 mL single dose at Visit 4, except participants in Norway and Denmark, who received a second dose of VARIVAX™ at Visit 5, according to local vaccination requirements).	
Reporting group title	Prevenar 13™
Reporting group description:	
Participants received a single 0.5 mL IM injection of Prevenar 13™ at Visit 1, 2, and 4 (approximately 3, 5, and 12 months of age). As part of the study design, participants also received other pediatric vaccines, including Vaxelis™ (0.5 mL single dose at Visits 1, 2, and 4); M-M-R™II (0.5 mL single dose at Visit 4); and VARIVAX™ (0.5 mL single dose at Visit 4, except participants in Norway and Denmark, who received a second dose of VARIVAX™ at Visit 5, according to local vaccination requirements).	

Reporting group values	V114	Prevenar 13™	Total
Number of subjects	595	596	1191
Age Categorical Units: Participants			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	595	596	1191
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: weeks			
arithmetic mean	12.4	12.5	
standard deviation	± 1.4	± 1.4	-
Gender Categorical Units: Participants			
Female	272	289	561
Male	323	307	630
Race Units: Subjects			
American Indian or Alaska Native	1	1	2
Asian	2	4	6
Multiple	13	12	25
White	579	579	1158
Ethnicity Units: Subjects			
Hispanic or Latino	26	22	48
Not Hispanic or Latino	564	570	1134

Not Reported	3	3	6
Unknown	2	1	3

End points

End points reporting groups

Reporting group title	V114
Reporting group description:	
Participants received a single 0.5 mL intramuscular (IM) injection of V114 at Visit 1, 2, and 4 (approximately 3, 5, and 12 months of age). As part of the study design, participants also received other pediatric vaccines, including Vaxelis™ (0.5 mL single dose at Visits 1, 2, and 4); M-M-R™II (0.5 mL single dose at Visit 4); and VARIVAX™ (0.5 mL single dose at Visit 4, except participants in Norway and Denmark, who received a second dose of VARIVAX™ at Visit 5, according to local vaccination requirements).	
Reporting group title	Prevenar 13™
Reporting group description:	
Participants received a single 0.5 mL IM injection of Prevenar 13™ at Visit 1, 2, and 4 (approximately 3, 5, and 12 months of age). As part of the study design, participants also received other pediatric vaccines, including Vaxelis™ (0.5 mL single dose at Visits 1, 2, and 4); M-M-R™II (0.5 mL single dose at Visit 4); and VARIVAX™ (0.5 mL single dose at Visit 4, except participants in Norway and Denmark, who received a second dose of VARIVAX™ at Visit 5, according to local vaccination requirements).	

Primary: Percentage of Participants with a Solicited Injection-site Adverse Event

End point title	Percentage of Participants with a Solicited Injection-site Adverse Event
End point description:	
An adverse event (AE) is any untoward medical occurrence in a clinical study participant, temporally associated with the use of study treatment, whether or not considered related to the study treatment. Solicited injection-site AEs included injection-site erythema (redness), injection-site induration (hard lump), injection-site pain (tenderness), and injection-site swelling. The analysis population for this endpoint included all randomized participants who received at least 1 dose of study vaccination.	
End point type	Primary
End point timeframe:	
Day 1 to Day 14 after each vaccination	

End point values	V114	Prevenar 13™		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	595	594		
Units: Percentage of participants				
number (not applicable)				
Injection-site erythema	60.0	65.5		
Injection-site induration	57.0	59.1		
Injection-site pain	63.0	59.6		
Injection-site swelling	46.4	44.1		

Statistical analyses

Statistical analysis title	Injection-site erythema
Comparison groups	Prevenar 13™ v V114

Number of subjects included in analysis	1189
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.05
Method	Miettinen & Nurminen method
Parameter estimate	Difference in percentage vs Prevenar 13™
Point estimate	-5.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11
upper limit	0

Statistical analysis title	Injection-site pain
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1189
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.225
Method	Miettinen & Nurminen method
Parameter estimate	Difference in percentage vs Prevenar 13™
Point estimate	3.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.1
upper limit	8.9

Statistical analysis title	Injection-site swelling
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1189
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.43
Method	Miettinen & Nurminen method
Parameter estimate	Difference in percentage vs Prevenar 13™
Point estimate	2.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.4
upper limit	7.9

Statistical analysis title	Injection-site induration

Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1189
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.46
Method	Miettinen & Nurminen method
Parameter estimate	Difference in percentage vs Prevenar 13™
Point estimate	-2.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.7
upper limit	3.5

Primary: Percentage of Participants with a Solicited Systemic Adverse Event

End point title	Percentage of Participants with a Solicited Systemic Adverse Event

End point description:

An AE is any untoward medical occurrence in a clinical study participant, temporally associated with the use of study treatment, whether or not considered related to the study treatment. Solicited systemic AEs included decreased appetite, irritability, somnolence (drowsiness), and urticaria (hives or welts). The analysis population for this endpoint included all randomized participants who received at least 1 dose of study vaccination.

End point type	Primary

End point timeframe:

Day 1 to Day 14 after each vaccination

End point values	V114	Prevenar 13™		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	595	594		
Units: Percentage of participants				
number (not applicable)				
Decreased appetite	54.8	58.2		
Irritability	96.3	94.1		
Somnolence	77.3	77.9		
Urticaria	16.8	21.4		

Statistical analyses

Statistical analysis title	Decreased appetite
Comparison groups	V114 v Prevenar 13™

Number of subjects included in analysis	1189
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.229
Method	Miettinen & Nurminen method
Parameter estimate	Difference in percentage vs Prevenar 13™
Point estimate	-3.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.1
upper limit	2.2

Statistical analysis title	Irritability
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1189
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.077
Method	Miettinen & Nurminen method
Parameter estimate	Difference in percentage vs Prevenar 13™
Point estimate	2.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	4.7

Statistical analysis title	Somnolence
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1189
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.793
Method	Miettinen & Nurminen method
Parameter estimate	Difference in percentage vs Prevenar 13™
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.4
upper limit	4.1

Statistical analysis title	Urticaria

Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1189
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.045
Method	Miettinen & Nurminen method
Parameter estimate	Difference in percentage vs Prevenar 13™
Point estimate	-4.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.1
upper limit	-0.1

Primary: Percentage of Participants with a Vaccine-related Serious Adverse Event

End point title	Percentage of Participants with a Vaccine-related Serious Adverse Event

End point description:

A serious adverse event (SAE) is an AE that results in death, 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. SAEs that were reported by the investigator to be at least possibly related to the study vaccination were summarized. The analysis population for this endpoint included all randomized participants who received at least 1 dose of study vaccination.

End point type	Primary

End point timeframe:

Up to approximately 6 months after Dose 3 (up to approximately 16 months)

End point values	V114	Prevenar 13™		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	595	594		
Units: Percentage of participants				
number (not applicable)	0.3	0.3		

Statistical analyses

Statistical analysis title	Vaccine-related SAEs
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1189
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen method
Parameter estimate	Difference in percentage vs Prevenar 13™
Point estimate	0

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	0.9

Primary: Percentage of Participants Meeting Serotype-specific Immunoglobulin G (IgG) Threshold Value of ≥0.35 µg/mL 30 Days after Dose 3

End point title	Percentage of Participants Meeting Serotype-specific Immunoglobulin G (IgG) Threshold Value of ≥0.35 µg/mL 30 Days after Dose 3

End point description:

The GMC of IgG serotype-specific antibodies to the 13 serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F) included in V114 and Prevenar 13™ and 2 serotypes (22F and 33F) unique to V114 were quantitated from participants' sera by a multiplex electrochemiluminescence (ECL) assay. Immunoglobulin G for the 15 serotypes contained in V114 vaccine was determined using a pneumococcal electrochemiluminescence (PnECL) assay. The analysis population for this endpoint included all randomized participants without protocol deviations that could have substantially impacted the results of the immunogenicity analyses and who had sufficient data to perform the analysis for each serotype.

End point type	Primary

End point timeframe:

30 days after Dose 3

End point values	V114	Prevenar 13™		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	500	525		
Units: Percentage of participants				
number (not applicable)				
Serotype 1 (n=500, 525)	96.8	99.0		
Serotype 3 (n=500, 525)	92.8	82.3		
Serotype 4 (n=500, 523)	96.6	98.5		
Serotype 5 (n=500, 524)	99.4	99.6		
Serotype 6A (n=500, 523)	99.2	99.4		
Serotype 6B (n=500, 523)	99.2	99.0		
Serotype 7F (n=500, 525)	100.0	99.6		
Serotype 9V (n=499, 525)	99.8	99.6		
Serotype 14 (n=500, 523)	99.2	99.6		
Serotype 18C (n=500, 525)	99.8	99.4		
Serotype 19A (n=500, 523)	99.6	99.8		
Serotype 19F (n=500, 524)	99.8	99.6		
Serotype 23F (n=497, 521)	97.8	96.9		
Serotype 22F (n=500, 520)	99.4	5.4		
Serotype 33F (n=500, 510)	99.2	2.0		

Statistical analyses

Statistical analysis title	Serotype 1
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1025
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	Miettinen & Nurminen method
Parameter estimate	Percentage point difference
Point estimate	-2.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.3
upper limit	-0.6

Statistical analysis title	Serotype 3
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1025
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	Miettinen & Nurminen method
Parameter estimate	Percentage point difference
Point estimate	10.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.6
upper limit	14.6

Statistical analysis title	Serotype 4
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1025
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	Miettinen & Nurminen method
Parameter estimate	Percentage point difference
Point estimate	-1.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4
upper limit	0

Statistical analysis title	Serotype 5
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1025
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	Miettinen & Nurminen method
Parameter estimate	Percentage point difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	0.8

Statistical analysis title	Serotype 6A
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1025
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	Miettinen & Nurminen method
Parameter estimate	Percentage point difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	1

Statistical analysis title	Serotype 6B
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1025
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	Miettinen & Nurminen method
Parameter estimate	Percentage point difference
Point estimate	0.2

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	1.5

Statistical analysis title	Serotype 7F
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1025
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	Miettinen & Nurminen method
Parameter estimate	Percentage point difference
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4
upper limit	1.4

Statistical analysis title	Serotype 9V
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1025
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	Miettinen & Nurminen method
Parameter estimate	Percentage point difference
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	1.2

Statistical analysis title	Serotype 14
Comparison groups	V114 v Prevenar 13™

Number of subjects included in analysis	1025
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	Miettinen & Nurminen method
Parameter estimate	Percentage point difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.7
upper limit	0.7

Statistical analysis title	Serotype 18C
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1025
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	Miettinen & Nurminen method
Parameter estimate	Percentage point difference
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	1.5

Statistical analysis title	Serotype 19A
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1025
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	Miettinen & Nurminen method
Parameter estimate	Percentage point difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	0.7

Statistical analysis title	Serotype 19F

Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1025
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	Miettinen & Nurminen method
Parameter estimate	Percentage point difference
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	1.2

Statistical analysis title	Serotype 23F
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1025
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	Miettinen & Nurminen method
Parameter estimate	Percentage point difference
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	3

Statistical analysis title	Serotype 22F
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1025
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Miettinen & Nurminen method
Parameter estimate	Percentage point difference
Point estimate	94
Confidence interval	
level	95 %
sides	2-sided
lower limit	91.6
upper limit	95.8

Statistical analysis title	Serotype 33F
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1025
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Miettinen & Nurminen method
Parameter estimate	Percentage point difference
Point estimate	97.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	95.4
upper limit	98.4

Primary: Geometric Mean Concentration (GMC) of Serotype-specific Immunoglobulin G (IgG) 30 Days after Dose 3

End point title	Geometric Mean Concentration (GMC) of Serotype-specific Immunoglobulin G (IgG) 30 Days after Dose 3

End point description:

The GMC of IgG serotype-specific antibodies to the 13 serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F) included in V114 and Prevenar 13™ and 2 serotypes (22F and 33F) unique to V114 were quantitated from participants' sera by a multiplex electrochemiluminescence (ECL) assay. The analysis population for this endpoint included all randomized participants without protocol deviations that could have substantially impacted the results of the immunogenicity analyses and who had sufficient data to perform the analysis for each serotype.

End point type	Primary

End point timeframe:

30 days after Dose 3

End point values	V114	Prevenar 13™		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	500	525		
Units: µg/mL				
geometric mean (confidence interval 95%)				
Serotype 1 (n=500, 525)	1.28 (1.21 to 1.36)	2.20 (2.08 to 2.34)		
Serotype 3 (n=500, 525)	0.85 (0.79 to 0.90)	0.65 (0.61 to 0.69)		
Serotype 4 (n=500, 523)	1.41 (1.31 to 1.51)	2.00 (1.86 to 2.16)		
Serotype 5 (n=500, 524)	2.08 (1.95 to 2.21)	3.35 (3.11 to 3.60)		
Serotype 6A (n=500, 523)	3.21 (2.97 to 3.47)	5.36 (4.98 to 5.78)		
Serotype 6B (n=500, 523)	4.56 (4.20 to 4.94)	5.12 (4.71 to 5.57)		
Serotype 7F (n=500, 525)	2.78 (2.64 to 2.94)	3.74 (3.53 to 3.97)		

Serotype 9V (n=499, 525)	2.14 (2.02 to 2.27)	3.07 (2.89 to 3.26)		
Serotype 14 (n=500, 523)	5.35 (4.93 to 5.80)	6.83 (6.33 to 7.37)		
Serotype 18C (n=500, 525)	2.10 (1.98 to 2.23)	2.48 (2.33 to 2.65)		
Serotype 19A (n=500, 523)	4.74 (4.43 to 5.08)	6.38 (5.96 to 6.83)		
Serotype 19F (n=500, 524)	4.08 (3.82 to 4.36)	5.18 (4.85 to 5.53)		
Serotype 23F (n=497, 521)	1.58 (1.47 to 1.70)	1.77 (1.64 to 1.91)		
Serotype 22F (n=500, 520)	6.06 (5.68 to 6.46)	0.09 (0.08 to 0.10)		
Serotype 33F (n=500, 510)	3.28 (3.06 to 3.51)	0.07 (0.06 to 0.07)		

Statistical analyses

Statistical analysis title	Serotype 3
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1025
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	t-test, 1-sided
Parameter estimate	GMC ratio
Point estimate	1.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.2
upper limit	1.43

Statistical analysis title	Serotype 1
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1025
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	t-test, 1-sided
Parameter estimate	GMC ratio
Point estimate	0.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.54
upper limit	0.63

Statistical analysis title	Serotype 4
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1025
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	t-test, 1-sided
Parameter estimate	GMC ratio
Point estimate	0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.63
upper limit	0.78

Statistical analysis title	Serotype 5
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1025
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	t-test, 1-sided
Parameter estimate	GMC ratio
Point estimate	0.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.56
upper limit	0.68

Statistical analysis title	Serotype 6A
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1025
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	t-test, 1-sided
Parameter estimate	GMC ratio
Point estimate	0.6

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.54
upper limit	0.67

Statistical analysis title	Serotype 7F
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1025
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	t-test, 1-sided
Parameter estimate	GMC ratio
Point estimate	0.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.69
upper limit	0.81

Statistical analysis title	Serotype 6B
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1025
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	t-test, 1-sided
Parameter estimate	GMC ratio
Point estimate	0.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.79
upper limit	1

Statistical analysis title	Serotype 9V
Comparison groups	V114 v Prevenar 13™

Number of subjects included in analysis	1025
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	t-test, 1-sided
Parameter estimate	GMC ratio
Point estimate	0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.64
upper limit	0.76

Statistical analysis title	Serotype 14
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1025
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	t-test, 1-sided
Parameter estimate	GMC ratio
Point estimate	0.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	0.87

Statistical analysis title	Serotype 18C
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1025
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	t-test, 1-sided
Parameter estimate	GMC ratio
Point estimate	0.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.77
upper limit	0.92

Statistical analysis title	Serotype 19A

Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1025
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	t-test, 1-sided
Parameter estimate	GMC ratio
Point estimate	0.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.68
upper limit	0.82

Statistical analysis title	Serotype 19F
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1025
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	t-test, 1-sided
Parameter estimate	GMC ratio
Point estimate	0.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.72
upper limit	0.87

Statistical analysis title	Serotype 23F
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1025
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	t-test, 1-sided
Parameter estimate	GMC ratio
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.81
upper limit	1

Statistical analysis title	Serotype 22F
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1025
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	t-test, 1-sided
Parameter estimate	GMC ratio
Point estimate	68.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	61.73
upper limit	75.65

Statistical analysis title	Serotype 33F
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1025
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	t-test, 1-sided
Parameter estimate	GMC ratio
Point estimate	48.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	44.45
upper limit	54.01

Secondary: Percentage of Participants Meeting Specified Vaxelis™ Antigen Reponses 30 Days after Dose 3

End point title	Percentage of Participants Meeting Specified Vaxelis™ Antigen Reponses 30 Days after Dose 3

End point description:

Antigen-specific response rates in participants administered V114 concomitantly with Vaxelis™ were compared with response rates in participants administered Prevenar 13™ concomitantly with Vaxelis™, and the percentages of participants meeting specified Vaxelis™ antigen responses recorded. Antigens in Vaxelis™ include: diphtheria toxoid, tetanus toxoid, pertussis toxin (PT), pertussis filamentous hemagglutinin (FHA), pertussis fimbriae 2/3 (FIM 2/3), pertussis pertactin (PRN), Haemophilus influenzae type b polyribosylribitol phosphate (Hib-PRP), hepatitis B surface antigen (HBsAg), and poliovirus serotypes 1, 2, and 3. The analysis population for this endpoint included all randomized participants without protocol deviations that could have substantially impacted the results of the immunogenicity analyses and who had sufficient data to perform the analysis for each serotype.

End point type	Secondary

End point timeframe:

30 days after Dose 3

End point values	V114	Prevenar 13™		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	500	525		
Units: Percentage of participants				
number (not applicable)				
Diphtheria toxoid: % ≥0.1 IU/mL (n=514, 543)	100.0	99.8		
Tetanus toxoid: % ≥0.1 IU/mL (n=514, 543)	100.0	99.8		
Pertussis - PT: % ≥5 EU/mL (n=514, 543)	100.0	99.8		
Pertussis - FHA: % ≥5 EU/mL (n=514, 543)	100.0	99.8		
Pertussis - FIM 2/3: % ≥20 EU/m L (n=514, 543)	99.8	99.6		
Pertussis - PRN: % ≥5 EU/mL (n=514, 543)	99.8	99.6		
Hib-PRP: % ≥0.15 µg/mL (n=495, 523)	96.8	97.9		
HBsAg: % ≥10 mIU/m L (n=495, 523)	99.0	99.6		
Poliovirus 1: % w/ Nab ≥1:8 dilution (n=502, 529)	99.8	99.8		
Poliovirus 2: % w/ Nab ≥1:8 dilution (n=499, 518)	100.0	99.8		
Poliovirus 3: % w/ Nab ≥1:8 dilution (n=503, 529)	100.0	100.0		

Statistical analyses

Statistical analysis title	Tetanus toxoid
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1025
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	Miettinen & Nurminen method
Parameter estimate	Percentage point difference
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	1

Statistical analysis title	Diphtheria toxoid
Comparison groups	V114 v Prevenar 13™

Number of subjects included in analysis	1025
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	Miettinen & Nurminen method
Parameter estimate	Percentage point difference
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	1

Statistical analysis title	Pertussis - PT
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1025
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	Miettinen & Nurminen method
Parameter estimate	Percentage point difference
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	1

Statistical analysis title	Pertussis - FIM 2/3
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1025
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	Miettinen & Nurminen method
Parameter estimate	Percentage point difference
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	1.2

Statistical analysis title	Pertussis - FHA

Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1025
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	Miettinen & Nurminen method
Parameter estimate	Percentage point difference
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	1

Statistical analysis title	Pertussis - PRN
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1025
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	Miettinen & Nurminen method
Parameter estimate	Percentage point difference
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	1.2

Statistical analysis title	Hib-PRP
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1025
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	Miettinen & Nurminen method
Parameter estimate	Percentage point difference
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.3
upper limit	0.9

Statistical analysis title	HBsAg
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1025
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	Miettinen & Nurminen method
Parameter estimate	Percentage point difference
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	0.5

Statistical analysis title	Poliovirus 1
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1025
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	Miettinen & Nurminen method
Parameter estimate	Percentage point difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	0.9

Statistical analysis title	Poliovirus 2
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1025
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	Miettinen & Nurminen method
Parameter estimate	Percentage point difference
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	1.1

Statistical analysis title	Poliovirus 3
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1025
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	Miettinen & Nurminen method
Parameter estimate	Percentage point difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	0.7

Secondary: Percentage of Participants Meeting Serotype-specific IgG Threshold Value of ≥0.35 µg/mL 30 Days after Dose 2

End point title	Percentage of Participants Meeting Serotype-specific IgG Threshold Value of ≥0.35 µg/mL 30 Days after Dose 2

End point description:

The GMC of IgG serotype-specific antibodies to the 13 serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F) included in V114 and Prevenar 13™ and 2 serotypes (22F and 33F) unique to V114 were quantitated from participants' sera by a multiplex ECL assay. Immunoglobulin G for the 15 serotypes contained in V114 vaccine was determined using a PnECL assay. The analysis population for this endpoint included all randomized participants without protocol deviations that could have substantially impacted the results of the immunogenicity analyses and who had sufficient data to perform the analysis for each serotype.

End point type	Secondary

End point timeframe:

30 days after Dose 2

End point values	V114	Prevenar 13™		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	505	499		
Units: Percentage of participants				
number (not applicable)				
Serotype 1 (n=505, 499)	97.2	98.2		
Serotype 3 (n=505, 499)	96.8	78.0		
Serotype 4 (n=505, 498)	97.6	98.2		
Serotype 5 (n=505, 498)	92.1	91.2		
Serotype 6A (n=505, 498)	77.2	91.4		
Serotype 6B (n=505, 499)	59.0	40.3		
Serotype 7F (n=505, 499)	98.6	99.8		
Serotype 9V (n=504, 498)	94.0	94.8		

Serotype 14 (n=504, 498)	96.6	96.0		
Serotype 18C (n=505, 499)	93.1	94.4		
Serotype 19A (n=505, 499)	94.1	96.6		
Serotype 19F (n=505, 499)	98.0	99.4		
Serotype 23F (n=505, 498)	75.4	66.7		
Serotype 22F (n=505, 499)	97.8	2.0		
Serotype 33F (n=505, 499)	49.5	1.6		

Statistical analyses

No statistical analyses for this end point

Secondary: GMC of Serotype-specific IgG 30 Days after Dose 2

End point title	GMC of Serotype-specific IgG 30 Days after Dose 2

End point description:

The GMC of IgG serotype-specific antibodies to the 13 serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F) included in V114 and Prevenar 13™ and 2 serotypes (22F and 33F) unique to V114 were quantitated from participants' sera by a multiplex ECL assay. Immunoglobulin G for the 15 serotypes contained in V114 vaccine was determined using a PnECL assay. The analysis population for this endpoint included all randomized participants without protocol deviations that could have substantially impacted the results of the immunogenicity analyses and who had sufficient data to perform the analysis for each serotype.

End point type	Secondary

End point timeframe:

30 days after Dose 2

End point values	V114	Prevenar 13™		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	505	499		
Units: µg/mL				
geometric mean (confidence interval 95%)				
Serotype 1 (n=505, 499)	1.39 (1.30 to 1.48)	1.70 (1.60 to 1.81)		
Serotype 3 (n=505, 499)	1.10 (1.04 to 1.17)	0.61 (0.57 to 0.65)		
Serotype 4 (n=505, 498)	1.74 (1.62 to 1.86)	1.59 (1.48 to 1.70)		
Serotype 5 (n=505, 498)	1.14 (1.05 to 1.23)	1.26 (1.16 to 1.37)		
Serotype 6A (n=505, 498)	0.67 (0.61 to 0.73)	1.53 (1.40 to 1.68)		
Serotype 6B (n=505, 499)	0.42 (0.37 to 0.48)	0.24 (0.22 to 0.27)		
Serotype 7F (n=505, 499)	1.69 (1.59 to 1.80)	2.18 (2.06 to 2.31)		
Serotype 9V (n=504, 498)	1.55 (1.43 to 1.68)	1.55 (1.43 to 1.67)		
Serotype 14 (n=504, 498)	5.59 (5.09 to 6.13)	5.48 (4.92 to 6.10)		

Serotype 18C (n=505,499)	1.18 (1.11 to 1.26)	1.58 (1.46 to 1.70)		
Serotype 19A (n=505, 499)	1.70 (1.56 to 1.84)	2.35 (2.15 to 2.56)		
Serotype 19F (n=505, 499)	2.79 (2.59 to 3.01)	4.04 (3.76 to 4.34)		
Serotype 23F (n=505, 498)	0.71 (0.65 to 0.78)	0.54 (0.49 to 0.59)		
Serotype 22F (n=505, 499)	3.16 (2.92 to 3.42)	0.04 (0.04 to 0.04)		
Serotype 33F (n=505, 499)	0.30 (0.27 to 0.34)	0.04 (0.04 to 0.04)		

Statistical analyses

Statistical analysis title	Serotype 3
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1004
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	1.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.66
upper limit	1.98

Statistical analysis title	Serotype 1
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1004
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	0.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.75
upper limit	0.89

Statistical analysis title	Serotype 5
Comparison groups	V114 v Prevenar 13™

Number of subjects included in analysis	1004
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	0.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.81
upper limit	1.01

Statistical analysis title	Serotype 4
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1004
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	1.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.99
upper limit	1.21

Statistical analysis title	Serotype 7F
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1004
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	0.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	0.84

Statistical analysis title	Serotype 6A
Comparison groups	V114 v Prevenar 13™

Number of subjects included in analysis	1004
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	0.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.38
upper limit	0.5

Statistical analysis title	Serotype 6B
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1004
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	1.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.46
upper limit	2.05

Statistical analysis title	Serotype 9V
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1004
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.9
upper limit	1.12

Statistical analysis title	Serotype 14
Comparison groups	V114 v Prevenar 13™

Number of subjects included in analysis	1004
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	1.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.89
upper limit	1.18

Statistical analysis title	Serotype 18C
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1004
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	0.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.68
upper limit	0.82

Statistical analysis title	Serotype 19A
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1004
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	0.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.64
upper limit	0.81

Statistical analysis title	Serotype 19F
Comparison groups	V114 v Prevenar 13™

Number of subjects included in analysis	1004
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	0.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.62
upper limit	0.77

Statistical analysis title	Serotype 23F
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1004
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	1.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.16
upper limit	1.51

Statistical analysis title	Serotype 22F
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1004
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	GMC ratio
Point estimate	81.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	73.12
upper limit	89.75

Statistical analysis title	Serotype 33F
Comparison groups	V114 v Prevenar 13™

Number of subjects included in analysis	1004
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC ratio
Point estimate	7.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.82
upper limit	8.94

Secondary: Percentage of Participants Meeting Specified Opsonophagocytic Activity (OPA) Responses 30 Days after Dose 3

End point title	Percentage of Participants Meeting Specified Opsonophagocytic Activity (OPA) Responses 30 Days after Dose 3

End point description:

OPA for the 13 serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F) included in V114 and Prevenar 13™ and 2 serotypes unique to V114 (22F and 33F) was measured using a multiplex opsonophagocytic assay (MOPA). The analysis population for this endpoint included all randomized participants in the OPA Subset without protocol deviations that could have substantially impacted the results of the immunogenicity analyses and who had sufficient data to perform the analysis for each serotype.

End point type	Secondary

End point timeframe:

30 days after Dose 3

End point values	V114	Prevenar 13™		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	108	95		
Units: Percentage of participants				
number (confidence interval 95%)				
Serotype 1: % ≥1:9 dilution (n=108, 94)	98.1 (93.5 to 99.8)	97.9 (92.5 to 99.7)		
Serotype 3: % ≥1:19 dilution (n=102, 92)	99.0 (94.7 to 100.0)	97.8 (92.4 to 99.7)		
Serotype 4: % ≥1:34 dilution (n=105, 92)	100.0 (96.5 to 100.0)	100.0 (96.1 to 100.0)		
Serotype 5: % ≥1:27 dilution (n=108, 95)	100.0 (96.6 to 100.0)	100.0 (96.2 to 100.0)		
Serotype 6A: % ≥1:232 dilution (n=100, 93)	100.0 (96.4 to 100.0)	100.0 (96.1 to 100.0)		
Serotype 6B: % ≥1:40 dilution (n=106, 93)	100.0 (96.6 to 100.0)	100.0 (96.1 to 100.0)		
Serotype 7F: % ≥1:61 dilution (n=106, 94)	100.0 (96.6 to 100.0)	100.0 (96.2 to 100.0)		
Serotype 9V: % ≥1:151 dilution (n=102, 91)	99.0 (94.7 to 100.0)	100.0 (96.0 to 100.0)		
Serotype 14: % ≥1:62 dilution (n=105, 93)	100.0 (96.5 to 100.0)	100.0 (96.1 to 100.0)		
Serotype 18C: % ≥1:115 dilution (n=104, 93)	99.0 (94.8 to 100.0)	100.0 (96.1 to 100.0)		

Serotype 19A : % ≥1:31 dilution (n=108, 93)	100.0 (96.6 to 100.0)	100.0 (96.1 to 100.0)		
Serotype 19F: % ≥1:113 dilution (n=104, 92)	100.0 (96.5 to 100.0)	100.0 (96.1 to 100.0)		
Serotype 23F: % ≥1:55 dilution (n=104, 91)	100.0 (96.5 to 100.0)	100.0 (96.0 to 100.0)		
Serotype 22F: % ≥1:15 dilution (n=104, 91)	100.0 (96.5 to 100.0)	26.4 (17.7 to 36.7)		
Serotype 33F: % ≥1:20 dilution (n=105, 95)	100.0 (96.5 to 100.0)	98.9 (94.3 to 100.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titers (GMTs) of Serotype-specific OPA 30 Days after Dose 3

End point title	Geometric Mean Titers (GMTs) of Serotype-specific OPA 30 Days after Dose 3

End point description:

Sera from participants was used to measure GMT of the 13 serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F) included in V114 and Prevenar 13™ and 2 serotypes unique to V114 (22F and 33F) was determined using a MOPA. The analysis population for this endpoint included all randomized participants in the OPA Subset without protocol deviations that could have substantially impacted the results of the immunogenicity analyses and who had sufficient data to perform the analysis for each serotype.

End point type	Secondary

End point timeframe:

30 days after Dose 3

End point values	V114	Prevenar 13™		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	108	95		
Units: Titer				
geometric mean (confidence interval 95%)				
Serotype 1 (n=108, 94)	152.2 (122.6 to 189.0)	184.0 (147.2 to 230.0)		
Serotype 3 (n=102, 92)	320.4 (266.9 to 384.8)	296.2 (245.5 to 357.3)		
Serotype 4 (n=105, 92)	2290.8 (1856.9 to 2826.1)	2842.0 (2404.6 to 3359.0)		
Serotype 5 (n=108, 95)	855.5 (699.9 to 1045.7)	1024.5 (850.5 to 1234.0)		
Serotype 6A (n=100, 93)	3316.8 (2828.4 to 3889.5)	4649.1 (3951.6 to 5469.7)		
Serotype 6B (n=106, 93)	2691.6 (2244.4 to 3227.8)	2658.7 (2234.2 to 3163.8)		

Serotype 7F (n=106, 94)	5819.2 (4985.3 to 6792.7)	7839.0 (6786.9 to 9054.2)		
Serotype 9V (n=102, 91)	2192.1 (1807.8 to 2658.1)	2745.1 (2284.2 to 3298.9)		
Serotype 14 (n=105, 93)	3449.4 (2803.1 to 4244.7)	2360.2 (1972.4 to 2824.3)		
Serotype 18C (n=104, 93)	2203.1 (1872.6 to 2592.1)	2003.4 (1725.7 to 2325.7)		
Serotype 19A (n=108, 93)	2839.1 (2455.2 to 3282.9)	3843.6 (3366.9 to 4387.8)		
Serotype 19F (n=104, 92)	1748.4 (1469.8 to 2079.7)	2067.0 (1800.1 to 2373.4)		
Serotype 23F (n= 104, 91)	3650.2 (3041.3 to 4381.0)	6776.2 (5344.0 to 8592.3)		
Serotype 22F (n=104, 91)	2927.9 (2547.0 to 3365.7)	29.3 (17.8 to 48.4)		
Serotype 33F (n=105, 95)	13334.7 (11334.6 to 15687.7)	1557.9 (1227.3 to 1977.5)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Non-serious AEs: up to 14 days after each vaccination dose; serious AEs and deaths (all causes): up to approximately 6 months after Dose 3 (up to approximately 16 months)

Adverse event reporting additional description:

The safety analysis population included all randomized participants who received at least 1 dose of study vaccination. The analysis population for number of deaths (all causes) included all randomized participants.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups

Reporting group title	V114

Reporting group description:

Participants received a single 0.5 mL intramuscular (IM) injection of V114 at Visit 1, 2, and 4 (approximately 3, 5, and 12 months of age). As part of the study design, participants also received other pediatric vaccines, including Vaxelis™ (0.5 mL single dose at Visits 1, 2, and 4); M-M-R™II (0.5 mL single dose at Visit 4); and VARIVAX™ (0.5 mL single dose at Visit 4, except participants in Norway and Denmark, who received a second dose of VARIVAX™ at Visit 5, according to local vaccination requirements).

Reporting group title	Prevenar 13™

Reporting group description:

Participants received a single 0.5 mL IM injection of Prevenar 13™ at Visit 1, 2 and 4 (approximately 3, 5, and 12 months of age). As part of the study design, participants also received other pediatric vaccines, including Vaxelis™ (0.5 mL single dose at Visits 1, 2, and 4); M-M-R™II (0.5 mL single dose at Visit 4); and VARIVAX™ (0.5 mL single dose at Visit 4, except participants in Norway and Denmark, who received a second dose of VARIVAX™ at Visit 5, according to local vaccination requirements).

Serious adverse events	V114	Prevenar 13™	
Total subjects affected by serious adverse events			
subjects affected / exposed	30 / 595 (5.04%)	28 / 594 (4.71%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Brain neoplasm			
subjects affected / exposed	1 / 595 (0.17%)	0 / 594 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Injury, poisoning and procedural complications			
Concussion			

subjects affected / exposed	1 / 595 (0.17%)	1 / 594 (0.17%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haemorrhage			
subjects affected / exposed	1 / 595 (0.17%)	0 / 594 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Laryngomalacia			
subjects affected / exposed	1 / 595 (0.17%)	0 / 594 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Febrile convulsion			
subjects affected / exposed	0 / 595 (0.00%)	1 / 594 (0.17%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsy			
subjects affected / exposed	1 / 595 (0.17%)	0 / 594 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infantile spasms			
subjects affected / exposed	1 / 595 (0.17%)	0 / 594 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Partial seizures			
subjects affected / exposed	0 / 595 (0.00%)	1 / 594 (0.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Petit mal epilepsy			
subjects affected / exposed	0 / 595 (0.00%)	1 / 594 (0.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Tremor			
subjects affected / exposed	1 / 595 (0.17%)	0 / 594 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	4 / 595 (0.67%)	2 / 594 (0.34%)	
occurrences causally related to treatment / all	2 / 4	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Food allergy			
subjects affected / exposed	1 / 595 (0.17%)	0 / 594 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 595 (0.17%)	1 / 594 (0.17%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	0 / 595 (0.00%)	1 / 594 (0.17%)	
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			
Adenoidal hypertrophy			
subjects affected / exposed	1 / 595 (0.17%)	0 / 594 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Tubulointerstitial nephritis			
subjects affected / exposed	0 / 595 (0.00%)	1 / 594 (0.17%)	
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			

Muscular weakness			
subjects affected / exposed	1 / 595 (0.17%)	0 / 594 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Arthritis infective			
subjects affected / exposed	1 / 595 (0.17%)	1 / 594 (0.17%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial infection			
subjects affected / exposed	1 / 595 (0.17%)	0 / 594 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchiolitis			
subjects affected / exposed	1 / 595 (0.17%)	0 / 594 (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	2 / 595 (0.34%)	1 / 594 (0.17%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis			
subjects affected / exposed	1 / 595 (0.17%)	0 / 594 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis adenovirus			
subjects affected / exposed	0 / 595 (0.00%)	1 / 594 (0.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	1 / 595 (0.17%)	2 / 594 (0.34%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngitis			

subjects affected / exposed	1 / 595 (0.17%)	3 / 594 (0.51%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pertussis			
subjects affected / exposed	1 / 595 (0.17%)	0 / 594 (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	1 / 595 (0.17%)	0 / 594 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia respiratory syncytial viral			
subjects affected / exposed	1 / 595 (0.17%)	0 / 594 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus bronchiolitis			
subjects affected / exposed	1 / 595 (0.17%)	3 / 594 (0.51%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	2 / 595 (0.34%)	2 / 594 (0.34%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus infection			
subjects affected / exposed	1 / 595 (0.17%)	1 / 594 (0.17%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	0 / 595 (0.00%)	1 / 594 (0.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhinitis			

subjects affected / exposed	0 / 595 (0.00%)	1 / 594 (0.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection viral			
subjects affected / exposed	0 / 595 (0.00%)	1 / 594 (0.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subcutaneous abscess			
subjects affected / exposed	1 / 595 (0.17%)	0 / 594 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 595 (0.17%)	0 / 594 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			
subjects affected / exposed	0 / 595 (0.00%)	2 / 594 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 595 (0.17%)	0 / 594 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Type 1 diabetes mellitus			
subjects affected / exposed	0 / 595 (0.00%)	1 / 594 (0.17%)	
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	Prevenar 13™	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	590 / 595 (99.16%)	592 / 594 (99.66%)	
Investigations			
Body temperature increased			
subjects affected / exposed	51 / 595 (8.57%)	61 / 594 (10.27%)	
occurrences (all)	74	91	
Nervous system disorders			
Somnolence			
subjects affected / exposed	460 / 595 (77.31%)	463 / 594 (77.95%)	
occurrences (all)	1118	1085	
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	357 / 595 (60.00%)	389 / 594 (65.49%)	
occurrences (all)	613	658	
Injection site pain			
subjects affected / exposed	375 / 595 (63.03%)	354 / 594 (59.60%)	
occurrences (all)	646	595	
Injection site induration			
subjects affected / exposed	339 / 595 (56.97%)	351 / 594 (59.09%)	
occurrences (all)	658	679	
Injection site swelling			
subjects affected / exposed	276 / 595 (46.39%)	262 / 594 (44.11%)	
occurrences (all)	444	417	
Pyrexia			
subjects affected / exposed	318 / 595 (53.45%)	330 / 594 (55.56%)	
occurrences (all)	728	762	
Gastrointestinal disorders			
Teething			
subjects affected / exposed	47 / 595 (7.90%)	50 / 594 (8.42%)	
occurrences (all)	60	67	
Diarrhoea			
subjects affected / exposed	69 / 595 (11.60%)	70 / 594 (11.78%)	
occurrences (all)	82	89	
Vomiting			
subjects affected / exposed	31 / 595 (5.21%)	38 / 594 (6.40%)	
occurrences (all)	38	41	

Skin and subcutaneous tissue disorders Urticaria subjects affected / exposed occurrences (all)	 100 / 595 (16.81%) 130	 127 / 594 (21.38%) 173	
Psychiatric disorders Irritability subjects affected / exposed occurrences (all)	 573 / 595 (96.30%) 2266	 559 / 594 (94.11%) 2304	
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	 70 / 595 (11.76%) 80	 84 / 594 (14.14%) 101	
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	 326 / 595 (54.79%) 632	 346 / 594 (58.25%) 686	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 October 2021	Amendment 03: The primary purpose of this amendment was to expand the visit windows for Visit 2 (Dose 2 vaccination), Visit 3 (post-dose 2 blood draw), Visit 4 (Dose 3 vaccination), and Visit 5 (post-dose 3 blood draw) to allow inclusion of more participants in the immunogenicity analysis based on the per-protocol population.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported