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 Infants (PNEU-PED-EU-1)

Summary

EudraCT number	2018-003787-31
Trial protocol	DE EE BE CZ ES PL GR Outside EU/EEA
Global end of trial date	05 August 2021

Results information

Result version number	v1 (current)
This version publication date	21 January 2022
First version publication date	21 January 2022

Trial information

Trial identification

Sponsor protocol code	V114-025

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04031846
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., Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-002215-PIP01-17
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	05 August 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	05 August 2021
Global end of trial reached?	Yes
Global end of trial date	05 August 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study evaluated the safety, tolerability and immunogenicity of V114, a 15-valent pneumococcal conjugate vaccine (PCV) when administered at ~ 2-months old. The primary hypotheses were: 1) V114 is non-inferior to Prevenar 13™, a 13-valent PCV, for the 13 shared serotypes between V114 and Prevenar 13™ based on response rates at 30 days post toddler dose (PTD); 2) V114 is superior to Prevenar 13™ for the 2 serotypes unique to V114 based on the response rates at 30 days PTD; 3) V114 is non-inferior to Prevenar 13™ for the 13 shared serotypes between V114 and Prevenar 13™ based on anti-pneumococcal polysaccharide (PnPs) serotype-specific Immunoglobin G (IgG) geometric mean concentrations (GMCs) at 30 days PTD; and 4) V114 is superior to Prevenar 13™ for the 2 serotypes unique to V114 based on anti-PnPs serotype-specific IgG GMCs at 30 days PTD.

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	04 September 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	Australia: 17
Country: Number of subjects enrolled	Belgium: 67
Country: Number of subjects enrolled	Czechia: 14
Country: Number of subjects enrolled	Estonia: 111
Country: Number of subjects enrolled	Germany: 187
Country: Number of subjects enrolled	Greece: 84
Country: Number of subjects enrolled	Poland: 316
Country: Number of subjects enrolled	Russian Federation: 20
Country: Number of subjects enrolled	Spain: 368
Worldwide total number of subjects	1184
EEA total number of subjects	1147

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)	1184
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:

Healthy males and females aged 42 to 90 days (inclusive) were enrolled. One participant randomized to the V114 group, who was cross-treated with both V114 and Prevenar 13™ (both PCVs), was excluded from the all participants as treated (APaT) i.e. the safety endpoints population; but was included in the AE module as a separate treatment group.

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	Subject, Investigator, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	V114

Arm description:

Full-term infants received a 0.5 mL intramuscular injection of V114 at approximately 2, 4, and 11-15 months of age (Study Day 1, Month 2, and Month 9-13). Preterm infants received a 0.5 mL intramuscular injection of V114 at approximately 2, 3, 4,and 11-15 months of age (Study Day 1, Month 1, Month 2, and Month 9-13). All infants also received licensed background intramuscular injections of 0.5 mL Infanrix™ hexa at approximately 2, 3, 4, and 11-15 months of age (Study Day 1, Months 1, 2, and Month 9-13); and also 1.5 mL oral dose of Rotarix™ at 2 and 4 months of age (Study Day 1 and Month 2).

Arm type	Experimental
Investigational medicinal product name	V114
Investigational medicinal product code	
Other name	VAXNEUVANCE™
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

15-valent PCV containing 13 serotypes present in Prevenar 13™ (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F) and 2 unique serotypes (22F and 33F) in each 0.5 mL intramuscular administration.

Investigational medicinal product name	Rotarix™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Single 1.5 mL oral dose at 2 and 4 months of age (Study Day 1 and Month 2).

Investigational medicinal product name	Infanrix™ hexa
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Single 0.5 mL intramuscular injection at 2, 3, 4, and 11-15 months of age (Study Day 1, Month 1, Month 2, and Month 9-13).

Arm title	Prevenar 13™

Arm description:

Full-term infants received a 0.5 mL intramuscular injection of Prevenar 13™ at approximately 2, 4, and 11-15 months of age (Study Day 1, Month 2, and Month 9-13). Preterm infants received a 0.5 mL intramuscular injection of Prevenar 13™ at approximately 2, 3, 4, and 11-15 months of age (Study Day 1, Month 1, Month 2, and Month 9-13). All infants also received licensed background intramuscular injections of 0.5 mL Infanrix™ hexa at approximately 2, 3, 4, and 11-15 months of age (Study Day 1, Months 1, 2, and Month 9-13); and also 1.5 mL oral dose of Rotarix™ at 2 and 4 months of age (Study Day 1 and Month 2).

Arm type	Active comparator
Investigational medicinal product name	Prevenar 13™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

13-valent PCV containing 13 serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A,19F, and 23F) in each 0.5 mL intramuscular administration.

Investigational medicinal product name	Infanrix™ hexa
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Single 0.5 mL intramuscular injection at 2, 3, 4, and 11-15 months of age (Study Day 1, Month 1, Month 2, and Month 9-13).

Investigational medicinal product name	Rotarix™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Single 1.5 mL oral dose at 2 and 4 months of age (Study Day 1 and Month 2).

Number of subjects in period 1	V114	Prevenar 13™
Started	591	593
Vaccinated	588	591
All Participants As Treated	587	591
PCV dose at age 2 months	588	591
PCV dose at age 3 months	32 [1]	35 [2]
PCV dose at age 4 months	582	584
PCV dose at age 11-14 months	571	574
Completed	569	570
Not completed	22	23
Physician decision	-	1
Withdrawal By Parent/Guardian	17	17
Lost to follow-up	4	4
Protocol deviation	1	1

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Due to a subset of participants receiving PCV at age 3 months, this resulted in lower numbers vaccinated.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Due to a subset of participants receiving PCV at age 3 months, this resulted in lower numbers vaccinated.

Baseline characteristics

Reporting groups	
Reporting group title	V114
Reporting group description:	
Full-term infants received a 0.5 mL intramuscular injection of V114 at approximately 2, 4, and 11-15 months of age (Study Day 1, Month 2, and Month 9-13). Preterm infants received a 0.5 mL intramuscular injection of V114 at approximately 2, 3, 4,and 11-15 months of age (Study Day 1, Month 1, Month 2, and Month 9-13). All infants also received licensed background intramuscular injections of 0.5 mL Infanrix™ hexa at approximately 2, 3, 4, and 11-15 months of age (Study Day 1, Months 1, 2, and Month 9-13); and also 1.5 mL oral dose of Rotarix™ at 2 and 4 months of age (Study Day 1 and Month 2).	
Reporting group title	Prevenar 13™
Reporting group description:	
Full-term infants received a 0.5 mL intramuscular injection of Prevenar 13™ at approximately 2, 4, and 11-15 months of age (Study Day 1, Month 2, and Month 9-13). Preterm infants received a 0.5 mL intramuscular injection of Prevenar 13™ at approximately 2, 3, 4, and 11-15 months of age (Study Day 1, Month 1, Month 2, and Month 9-13). All infants also received licensed background intramuscular injections of 0.5 mL Infanrix™ hexa at approximately 2, 3, 4, and 11-15 months of age (Study Day 1, Months 1, 2, and Month 9-13); and also 1.5 mL oral dose of Rotarix™ at 2 and 4 months of age (Study Day 1 and Month 2).	

Reporting group values	V114	Prevenar 13™	Total
Number of subjects	591	593	1184
Age Categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	591	593	1184
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	8.4	8.5	
standard deviation	± 1.5	± 1.5	-
Gender Categorical Units: Subjects			
Female	283	286	569
Male	308	307	615
Race Categorical Units: Subjects			
American Indian Or Alaska Native	4	5	9
Asian	4	5	9
Black Or African American	4	3	7
Multiple	5	7	12
White	574	573	1147
Ethnicity Categorical			

Units: Subjects			
Hispanic Or Latino	66	65	131
Not Hispanic Or Latino	525	526	1051
Not Reported	0	1	1
Unknown	0	1	1

End points

End points reporting groups

Reporting group title	V114

Reporting group description:

Full-term infants received a 0.5 mL intramuscular injection of V114 at approximately 2, 4, and 11-15 months of age (Study Day 1, Month 2, and Month 9-13). Preterm infants received a 0.5 mL intramuscular injection of V114 at approximately 2, 3, 4,and 11-15 months of age (Study Day 1, Month 1, Month 2, and Month 9-13). All infants also received licensed background intramuscular injections of 0.5 mL Infanrix™ hexa at approximately 2, 3, 4, and 11-15 months of age (Study Day 1, Months 1, 2, and Month 9-13); and also 1.5 mL oral dose of Rotarix™ at 2 and 4 months of age (Study Day 1 and Month 2).

Reporting group title	Prevenar 13™

Reporting group description:

Full-term infants received a 0.5 mL intramuscular injection of Prevenar 13™ at approximately 2, 4, and 11-15 months of age (Study Day 1, Month 2, and Month 9-13). Preterm infants received a 0.5 mL intramuscular injection of Prevenar 13™ at approximately 2, 3, 4, and 11-15 months of age (Study Day 1, Month 1, Month 2, and Month 9-13). All infants also received licensed background intramuscular injections of 0.5 mL Infanrix™ hexa at approximately 2, 3, 4, and 11-15 months of age (Study Day 1, Months 1, 2, and Month 9-13); and also 1.5 mL oral dose of Rotarix™ at 2 and 4 months of age (Study Day 1 and Month 2).

Primary: Percentage of Participants That Report at Least 1 Solicited Injection-site Adverse Event (AE)

End point title	Percentage of Participants That Report at Least 1 Solicited Injection-site Adverse Event (AE)

End point description:

An AE is any untoward medical occurrence in a participant temporally associated with the use of a study intervention, whether or not considered related to the study intervention. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom or disease (new or exacerbated) temporally associated with the use of a study intervention. Injection-site AEs solicited on the Vaccine Report Card (VRC) consisted of erythema (redness), induration (hard lump), pain (tenderness) and swelling. The population analyzed was All Participants as Treated (APat) which consisted of participants who received at least 1 dose of study vaccination based on the group to which they were randomized, and corresponding to the study vaccination they actually received. One participant randomized to V114, who inadvertently received both V114 and Prevenar 13™, was excluded from this analysis.

End point type	Primary

End point timeframe:

Up to 14 days post any vaccination (up to approximately study month 13)

End point values	V114	Prevenar 13™		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	587	591		
Units: Percentage of Participants				
number (not applicable)				
Injection site erythema	45.3	44.7		
Injection site induration	41.9	39.1		
Injection site pain	40.5	29.3		
Injection site swelling	33.6	29.4		

Statistical analyses

Statistical analysis title	P-value and Diff. in %: Inj. site erythema
Statistical analysis description:	
Difference in % (V114 minus Prevenar 13™) and 95 % confidence interval (CI) are calculated based on the Miettinen & Nurminen method.	
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1178
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.824
Method	Miettinen & Nurminen
Parameter estimate	Percentage Difference
Point estimate	0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5
upper limit	6.3

Statistical analysis title	P-value and Diff. in %:: Inj. site induration
Statistical analysis description:	
Difference in % (V114 minus Prevenar 13™) and 95 % CI are calculated based on the Miettinen & Nurminen method.	
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1178
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.324
Method	Miettinen & Nurminen
Parameter estimate	Percentage Difference
Point estimate	2.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.8
upper limit	8.4

Statistical analysis title	P-value and Diff. in %: Inj. site pain
Statistical analysis description:	
Difference in % (V114 minus Prevenar 13™) and 95 % CI are calculated based on the Miettinen &	

Nurminen method.

Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1178
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Percentage Difference
Point estimate	11.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.8
upper limit	16.6

Statistical analysis title	P-value and Diff. in %: Inj. site swelling

Statistical analysis description:

Difference in % (V114 minus Prevenar 13™) and 95 % CI are calculated based on the Miettinen & Nurminen method.

Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1178
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.128
Method	Miettinen & Nurminen
Parameter estimate	Percentage Difference
Point estimate	4.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	9.4

Primary: Percentage of Participants that Report at Least 1 Solicited Systemic AE

End point title	Percentage of Participants that Report at Least 1 Solicited Systemic AE

End point description:

An AE is any untoward medical occurrence in a participant temporally associated with the use of a study intervention, whether or not considered related to the study intervention. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom or disease (new or exacerbated) temporally associated with the use of a study intervention. Systemic AEs solicited on the VRC consisted of decreased appetite (loss of appetite), irritability, somnolence (drowsiness) and urticaria (hive/welts). The population analyzed was APat which consisted of participants who received at least 1 dose of study vaccination based on the group to which they were randomized, and corresponding to the study vaccination they actually received. One participant randomized to V114, who inadvertently received both V114 and Prevenar 13™, was excluded from this analysis.

End point type	Primary

End point timeframe:

Up to 14 days post any vaccination (up to approximately study month 13)

End point values	V114	Prevenar 13™		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	587	591		
Units: Percentage of Participants				
number (not applicable)				
Decreased appetite	33.9	33.5		
Irritability	71.7	66.3		
Somnolence	46.2	41.8		
Urticaria	3.7	3.9		

Statistical analyses

Statistical analysis title	P-value and Diff. in %: Decreased appetite
Statistical analysis description:	
Difference in % (V114 minus Prevenar 13™) and 95 % CI are calculated based on the Miettinen & Nurminen method.	
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1178
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.885
Method	Miettinen & Nurminen
Parameter estimate	Percentage Difference
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5
upper limit	5.8

Statistical analysis title	P-value and Diff. in %: Irritability
Statistical analysis description:	
Difference in % (V114 minus Prevenar 13™) and 95 % CI are calculated based on the Miettinen & Nurminen method.	
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1178
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.045
Method	Miettinen & Nurminen
Parameter estimate	Percentage Difference
Point estimate	5.4

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.1
upper limit	10.7

Statistical analysis title	P-value and Diff. in %: Somnolence
Statistical analysis description:	
Difference in % (V114 minus Prevenar 13™) and 95 % CI are calculated based on the Miettinen & Nurminen method.	
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1178
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.131
Method	Miettinen & Nurminen
Parameter estimate	Percentage Difference
Point estimate	4.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	10

Statistical analysis title	P-value and Diff. in %: Urticaria
Statistical analysis description:	
Difference in % (V114 minus Prevenar 13™) and 95 % CI are calculated based on the Miettinen & Nurminen method.	
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1178
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.898
Method	Miettinen & Nurminen
Parameter estimate	Percentage Difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.4
upper limit	2.1

Primary: Percentage of Participants That Report at Least 1 Vaccine-related Serious Adverse Event (SAE)

End point title	Percentage of Participants That Report at Least 1 Vaccine-

	related Serious Adverse Event (SAE)

End point description:

A serious adverse event (SAE) is an AE that results in death, is life threatening, results in a persistent or significant disability or incapacity, results in or prolongs an existing hospitalization, is a congenital anomaly or birth defect, is a cancer, is an overdose, or is another important medical event. The relatedness of a vaccine to a SAE is determined by an investigator who is a qualified physician. The population analyzed was APat which consisted of participants who received at least 1 dose of study vaccination based on the group to which they were randomized, and corresponding to the study vaccination they actually received. One participant randomized to V114, who inadvertently received both V114 and Prevenar 13™, was excluded from this analysis.

End point type	Primary

End point timeframe:

Up to 6 months post last vaccination (up to approximately study month 20)

End point values	V114	Prevenar 13™		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	587	591		
Units: Percentage of Participants				
number (not applicable)	0.0	0.2		

Statistical analyses

Statistical analysis title	Difference in % vs Prevenar 13™

Statistical analysis description:

Percentage of participants from V114 minus Prevenar 13™. Difference in % and 95 % CI are calculated based on the Miettinen & Nurminen method.

Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1178
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Percentage Difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	0.5

Primary: Anti-pneumococcal Polysaccharide (PnPs) Serotype-specific Immunoglobin G (IgG) Geometric Mean Concentrations (GMC) for Each Serotype at 30 Days Post Toddler Dose (PTD)

End point title	Anti-pneumococcal Polysaccharide (PnPs) Serotype-specific Immunoglobin G (IgG) Geometric Mean Concentrations (GMC) for Each Serotype at 30 Days Post Toddler Dose (PTD)

End point description:

Sera from participants was used to measure vaccine-induced anti-PnPs serotype-specific IgG for each serotype using pneumococcal electrochemiluminescence (PnECL). The Geometric Mean Concentration

(GMC) for each of the 13 serotypes shared by both V114 and Prevenar 13™ (Serotypes 1 to 23F); and the 2 serotypes unique to V114 (Serotypes 22F and 33F) was assessed. The population analyzed consisted of all randomized participants without deviations from the protocol that may substantially affect the results. Deviations that affect the number analyzed include, but are not limited to, failure to receive vaccination; receipt of prohibited medication or vaccine; failure to receive vaccination at the required time point; failure to receive the required vaccination dose; and collection of blood sample at a time point outside of the prespecified time window.

End point type	Primary

End point timeframe:

30 days PTD (Up to approximately study month 14)

End point values	V114	Prevenar 13™		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	588	591		
Units: µg/mL				
number (not applicable)				
Serotype 1 (n= 539, 537)	1.29	2.08		
Serotype 3 (n= 539, 537)	0.84	0.66		
Serotype 4 (n= 539, 535)	1.29	1.73		
Serotype 5 (n= 539, 535)	1.97	3.06		
Serotype 6A (n= 539, 535)	3.10	4.57		
Serotype 6B (n= 539, 535)	4.17	4.37		
Serotype 7F (n= 539, 536)	3.09	3.93		
Serotype 9V (n= 539, 537)	2.14	2.99		
Serotype 14 (n= 539, 537)	5.26	7.04		
Serotype 18C (n= 539, 536)	1.94	2.22		
Serotype 19A (n= 539, 535)	4.68	5.65		
Serotype 19F (n= 539, 537)	4.09	4.63		
Serotype 23F (n= 538, 535)	1.52	1.75		
Serotype 22F (n= 539, 535)	5.98	0.08		
Serotype 33F (n= 539, 530)	3.41	0.07		

Statistical analyses

Statistical analysis title	GMC Ratio : Serotype 1

Statistical analysis description:

GMC ratio (V114/Prevenar 13™), CI, and p-value are calculated using the t-distribution with the variance estimate from a serotype-specific linear model utilizing the natural log-transformed antibody concentrations as the response and a single term for vaccination group.

Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
P-value	< 0.001 [2]
Method	t-distribution
Parameter estimate	GMC Ratio
Point estimate	0.62

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.57
upper limit	0.68

Notes:

[1] - Non-inferiority of V114 to Prevenar 13™ is based on the lower bound of the 2-sided 95% CI for the GMC ratio (V114/Prevenar 13™) being >0.5 (1-sided p-value <0.025).
[2] - 1-sided p-value

Statistical analysis title	GMC Ratio : Serotype 3

Statistical analysis description:

GMC ratio (V114/Prevenar 13™), CI, and p-value are calculated using the t-distribution with the variance estimate from a serotype-specific linear model utilizing the natural log-transformed antibody concentrations as the response and a single term for vaccination group.

Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
P-value	< 0.001 [4]
Method	t-distribution
Parameter estimate	GMC Ratio
Point estimate	1.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.17
upper limit	1.39

Notes:

[3] - Non-inferiority of V114 to Prevenar 13™ is based on the lower bound of the 2-sided 95% CI for the GMC ratio (V114/Prevenar 13™) being >0.5 (1-sided p-value <0.025).
[4] - 1-sided p-value

Statistical analysis title	GMC Ratio : Serotype 4

Statistical analysis description:

GMC ratio (V114/Prevenar 13™), CI, and p-value are calculated using the t-distribution with the variance estimate from a serotype-specific linear model utilizing the natural log-transformed antibody concentrations as the response and a single term for vaccination group.

Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	non-inferiority[5]
P-value	< 0.001 [6]
Method	t-distribution
Parameter estimate	GMC Ratio
Point estimate	0.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.68
upper limit	0.82

Notes:

[5] - Non-inferiority of V114 to Prevenar 13™ is based on the lower bound of the 2-sided 95% CI for the GMC ratio (V114/Prevenar 13™) being >0.5 (1-sided p-value <0.025).

[6] - 1-sided p-value

Statistical analysis title	GMC Ratio : Serotype 5

Statistical analysis description:

GMC ratio (V114/Prevenar 13™), CI, and p-value are calculated using the t-distribution with the variance estimate from a serotype-specific linear model utilizing the natural log-transformed antibody concentrations as the response and a single term for vaccination group.

Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	non-inferiority[7]
P-value	< 0.001 [8]
Method	t-distribution
Parameter estimate	GMC Ratio
Point estimate	0.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.59
upper limit	0.7

Notes:

[7] - Non-inferiority of V114 to Prevenar 13™ is based on the lower bound of the 2-sided 95% CI for the GMC ratio (V114/Prevenar 13™) being >0.5 (1-sided p-value <0.025).
[8] - 1-sided p-value

Statistical analysis title	GMC Ratio : Serotype 6A

Statistical analysis description:

GMC ratio (V114/Prevenar 13™), CI, and p-value are calculated using the t-distribution with the variance estimate from a serotype-specific linear model utilizing the natural log-transformed antibody concentrations as the response and a single term for vaccination group.

Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	non-inferiority[9]
P-value	< 0.001 [10]
Method	t-distribution
Parameter estimate	GMC Ratio
Point estimate	0.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.61
upper limit	0.76

Notes:

[9] - Non-inferiority of V114 to Prevenar 13™ is based on the lower bound of the 2-sided 95% CI for the GMC ratio (V114/Prevenar 13™) being >0.5 (1-sided p-value <0.025).
[10] - 1-sided p-value

Statistical analysis title	GMC Ratio : Serotype 6B

Statistical analysis description:

GMC ratio (V114/Prevenar 13™), CI, and p-value are calculated using the t-distribution with the variance estimate from a serotype-specific linear model utilizing the natural log-transformed antibody concentrations as the response and a single term for vaccination group.

Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	non-inferiority[11]
P-value	< 0.001 [12]
Method	t-distribution
Parameter estimate	GMC Ratio
Point estimate	0.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.85
upper limit	1.07

Notes:

[11] - Non-inferiority of V114 to Prevenar 13™ is based on the lower bound of the 2-sided 95% CI for the GMC ratio (V114/Prevenar 13™) being >0.5 (1-sided p-value <0.025).
[12] - 1-sided p-value

Statistical analysis title	GMC Ratio : Serotype 7F

Statistical analysis description:

GMC ratio (V114/Prevenar 13™), CI, and p-value are calculated using the t-distribution with the variance estimate from a serotype-specific linear model utilizing the natural log-transformed antibody concentrations as the response and a single term for vaccination group.

Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	non-inferiority[13]
P-value	< 0.001 [14]
Method	t-distribution
Parameter estimate	GMC Ratio
Point estimate	0.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.72
upper limit	0.85

Notes:

[13] - Non-inferiority of V114 to Prevenar 13™ is based on the lower bound of the 2-sided 95% CI for the GMC ratio (V114/Prevenar 13™) being >0.5 (1-sided p-value <0.025).
[14] - 1-sided p-value

Statistical analysis title	GMC Ratio : Serotype 9V

Statistical analysis description:

GMC ratio (V114/Prevenar 13™), CI, and p-value are calculated using the t-distribution with the variance estimate from a serotype-specific linear model utilizing the natural log-transformed antibody concentrations as the response and a single term for vaccination group.

Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	non-inferiority[15]
P-value	< 0.001 [16]
Method	t-distribution
Parameter estimate	GMC Ratio
Point estimate	0.72

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.66
upper limit	0.78

Notes:

[15] - Non-inferiority of V114 to Prevenar 13™ is based on the lower bound of the 2-sided 95% CI for the GMC ratio (V114/Prevenar 13™) being >0.5 (1-sided p-value <0.025).
[16] - 1-sided p-value

Statistical analysis title	GMC Ratio : Serotype 14

Statistical analysis description:

GMC ratio (V114/Prevenar 13™), CI, and p-value are calculated using the t-distribution with the variance estimate from a serotype-specific linear model utilizing the natural log-transformed antibody concentrations as the response and a single term for vaccination group.

Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	non-inferiority[17]
P-value	< 0.001 [18]
Method	t-distribution
Parameter estimate	GMC Ratio
Point estimate	0.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.67
upper limit	0.83

Notes:

[17] - Non-inferiority of V114 to Prevenar 13™ is based on the lower bound of the 2-sided 95% CI for the GMC ratio (V114/Prevenar 13™) being >0.5 (1-sided p-value <0.025).
[18] - 1-sided p-value

Statistical analysis title	GMC Ratio : Serotype 18C

Statistical analysis description:

GMC ratio (V114/Prevenar 13™), CI, and p-value are calculated using the t-distribution with the variance estimate from a serotype-specific linear model utilizing the natural log-transformed antibody concentrations as the response and a single term for vaccination group.

Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	non-inferiority[19]
P-value	< 0.001 [20]
Method	t-distribution
Parameter estimate	GMC Ratio
Point estimate	0.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8
upper limit	0.95

Notes:

[19] - Non-inferiority of V114 to Prevenar 13™ is based on the lower bound of the 2-sided 95% CI for the GMC ratio (V114/Prevenar 13™) being >0.5 (1-sided p-value <0.025).

[20] - 1-sided p-value

Statistical analysis title	GMC Ratio : Serotype 19A

Statistical analysis description:

GMC ratio (V114/Prevenar 13™), CI, and p-value are calculated using the t-distribution with the variance estimate from a serotype-specific linear model utilizing the natural log-transformed antibody concentrations as the response and a single term for vaccination group.

Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	non-inferiority[21]
P-value	< 0.001 [22]
Method	t-distribution
Parameter estimate	GMC Ratio
Point estimate	0.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.75
upper limit	0.91

Notes:

[21] - Non-inferiority of V114 to Prevenar 13™ is based on the lower bound of the 2-sided 95% CI for the GMC ratio (V114/Prevenar 13™) being >0.5 (1-sided p-value <0.025).
[22] - 1-sided p-value

Statistical analysis title	GMC Ratio : Serotype 19F

Statistical analysis description:

GMC ratio (V114/Prevenar 13™), CI, and p-value are calculated using the t-distribution with the variance estimate from a serotype-specific linear model utilizing the natural log-transformed antibody concentrations as the response and a single term for vaccination group.

Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	non-inferiority[23]
P-value	< 0.001 [24]
Method	t-distribution
Parameter estimate	GMC Ratio
Point estimate	0.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8
upper limit	0.97

Notes:

[23] - Non-inferiority of V114 to Prevenar 13™ is based on the lower bound of the 2-sided 95% CI for the GMC ratio (V114/Prevenar 13™) being >0.5 (1-sided p-value <0.025).
[24] - 1-sided p-value

Statistical analysis title	GMC Ratio : Serotype 23F

Statistical analysis description:

GMC ratio (V114/Prevenar 13™), CI, and p-value are calculated using the t-distribution with the variance estimate from a serotype-specific linear model utilizing the natural log-transformed antibody concentrations as the response and a single term for vaccination group.

Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	non-inferiority[25]
P-value	< 0.001 [26]
Method	t-distribution
Parameter estimate	GMC Ratio
Point estimate	0.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.79
upper limit	0.97

Notes:

[25] - Non-inferiority of V114 to Prevenar 13™ is based on the lower bound of the 2-sided 95% CI for the GMC ratio (V114/Prevenar 13™) being >0.5 (1-sided p-value <0.025).
[26] - 1-sided p-value

Statistical analysis title	GMC Ratio : Serotype 22F

Statistical analysis description:

GMC ratio (V114/Prevenar 13™), CI, and p-value are calculated using the t-distribution with the variance estimate from a serotype-specific linear model utilizing the natural log-transformed antibody concentrations as the response and a single term for vaccination group.

Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	superiority[27]
P-value	< 0.001 [28]
Method	t-distribution
Parameter estimate	GMC Ratio
Point estimate	71.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	65.16
upper limit	79.1

Notes:

[27] - Superiority of V114 to Prevenar 13™ is based on the lower bound of the 2-sided 95% CI for the GMC ratio (V114/Prevenar 13™) being >2.0 (1-sided p-value <0.025).
[28] - 1-sided p-value

Statistical analysis title	GMC Ratio : Serotype 33F

Statistical analysis description:

GMC ratio (V114/Prevenar 13™), CI, and p-value are calculated using the t-distribution with the variance estimate from a serotype-specific linear model utilizing the natural log-transformed antibody concentrations as the response and a single term for vaccination group.

Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	superiority[29]
P-value	< 0.001 [30]
Method	t-distribution
Parameter estimate	GMC Ratio
Point estimate	46.58

Confidence interval	
level	95 %
sides	2-sided
lower limit	42.19
upper limit	51.42

Notes:

[29] - Superiority of V114 to Prevenar 13™ is based on the lower bound of the 2-sided 95% CI for the GMC ratio (V114/Prevenar 13™) being >2.0 (1-sided p-value <0.025).
[30] - 1-sided p-value

Primary: Percentage of Participants Who Meet Serotype-specific IgG Threshold Value of ≥0.35 µg/mL for Each Serotype at 30 Days PTD

End point title	Percentage of Participants Who Meet Serotype-specific IgG Threshold Value of ≥0.35 µg/mL for Each Serotype at 30 Days PTD

End point description:

Sera from participants was used to measure vaccine-induced anti-PnPs serotype-specific IgG for the 15 serotypes using pneumococcal electrochemiluminescence (PnECL). The percentage of participants that achieve the threshold value of ≥0.35 µg/mL for each of the 13 serotypes shared by both V114 and Prevenar 13™ (Serotypes 1 to 23F); and the 2 serotypes unique to V114 (Serotypes 22F and 33F) was assessed. The population analyzed consisted of all randomized participants without deviations from the protocol that may substantially affect the results. Deviations that affect the number analyzed include, but are not limited to, failure to receive vaccination; receipt of prohibited medication or vaccine; failure to receive vaccination at the required time point; failure to receive the required vaccination dose; and collection of blood sample at a time point outside of the prespecified time window.

End point type	Primary

End point timeframe:

30 days PTD (Up to approximately study month 14)

End point values	V114	Prevenar 13™		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	588	591		
Units: Percentage of Participants				
number (not applicable)				
Serotype 1 (n= 539, 537)	96.7	99.4		
Serotype 3 (n= 539, 537)	92.0	83.8		
Serotype 4 (n= 539, 535)	95.7	97.9		
Serotype 5 (n= 539, 535)	99.1	100.0		
Serotype 6A (n= 539, 535)	98.5	98.9		
Serotype 6B (n= 539, 535)	97.4	99.1		
Serotype 7F (n= 539, 536)	99.8	99.8		
Serotype 9V (n= 539, 537)	98.9	100.0		
Serotype 14 (n= 539, 537)	99.8	100.0		
Serotype 18C (n= 539, 536)	98.9	99.3		
Serotype 19A (n= 539, 535)	99.1	100.0		
Serotype 19F (n= 539, 537)	99.6	100.0		
Serotype 23F (n= 538, 535)	96.8	97.4		
Serotype 22F (n= 539, 535)	99.6	5.8		
Serotype 33F (n= 539, 530)	99.1	4.2		

Statistical analyses

Statistical analysis title	Percentage Difference : Serotype 1
Statistical analysis description:	
Percentage difference (V114 minus Prevenar 13™), CI, and p-value are based on the Miettinen & Nurminen method.	
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	non-inferiority[31]
P-value	< 0.001 [32]
Method	Miettinen & Nurminen
Parameter estimate	Percentage Difference
Point estimate	-2.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.7
upper limit	-1.3

Notes:

[31] - Non-inferiority of V114 to Prevenar 13™ is based on the lower bound of the 95% CI for the difference in percentages (V114 - Prevenar 13™) being >-10 percentage points (1-sided p-value <0.025).
[32] - 1-sided p-value

Statistical analysis title	Percentage Difference : Serotype 3
Statistical analysis description:	
Percentage difference (V114 minus Prevenar 13™), CI, and p-value are based on the Miettinen & Nurminen method.	
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	non-inferiority[33]
P-value	< 0.001 [34]
Method	Miettinen & Nurminen
Parameter estimate	Percentage Difference
Point estimate	8.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.4
upper limit	12.2

Notes:

[33] - Non-inferiority of V114 to Prevenar 13™ is based on the lower bound of the 95% CI for the difference in percentages (V114 - Prevenar 13™) being >-10 percentage points (1-sided p-value <0.025).

[34] - 1-sided p-value

Statistical analysis title	Percentage Difference : Serotype 4
Statistical analysis description:	
Percentage difference (V114 minus Prevenar 13™), CI, and p-value are based on the Miettinen & Nurminen method.	
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	non-inferiority[35]
P-value	< 0.001 [36]
Method	Miettinen & Nurminen
Parameter estimate	Percentage Difference
Point estimate	-2.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.5
upper limit	-0.1

Notes:

[35] - Non-inferiority of V114 to Prevenar 13™ is based on the lower bound of the 95% CI for the difference in percentages (V114 - Prevenar 13™) being >-10 percentage points (1-sided p-value <0.025).
[36] - 1-sided p-value

Statistical analysis title	Percentage Difference : Serotype 5
Statistical analysis description:	
Percentage difference (V114 minus Prevenar 13™), CI, and p-value are based on the Miettinen & Nurminen method.	
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	non-inferiority[37]
P-value	< 0.001 [38]
Method	Miettinen & Nurminen
Parameter estimate	Percentage Difference
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.2
upper limit	-0.2

Notes:

[37] - Non-inferiority of V114 to Prevenar 13™ is based on the lower bound of the 95% CI for the difference in percentages (V114 - Prevenar 13™) being >-10 percentage points (1-sided p-value <0.025).
[38] - 1-sided p-value

Statistical analysis title	Percentage Difference : Serotype 6A
Statistical analysis description:	
Percentage difference (V114 minus Prevenar 13™), CI, and p-value are based on the Miettinen & Nurminen method.	
Comparison groups	V114 v Prevenar 13™

Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	non-inferiority[39]
P-value	< 0.001 [40]
Method	Miettinen & Nurminen
Parameter estimate	Percentage Difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.9
upper limit	1.1

Notes:

[39] - Non-inferiority of V114 to Prevenar 13™ is based on the lower bound of the 95% CI for the difference in percentages (V114 - Prevenar 13™) being >-10 percentage points (1-sided p-value <0.025).

[40] - 1-sided p-value

Statistical analysis title	Percentage Difference : Serotype 6B

Statistical analysis description:

Percentage difference (V114 minus Prevenar 13™), CI, and p-value are based on the Miettinen & Nurminen method.

Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	non-inferiority[41]
P-value	< 0.001 [42]
Method	Miettinen & Nurminen
Parameter estimate	Percentage Difference
Point estimate	-1.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.5
upper limit	-0.1

Notes:

[41] - Non-inferiority of V114 to Prevenar 13™ is based on the lower bound of the 95% CI for the difference in percentages (V114 - Prevenar 13™) being >-10 percentage points (1-sided p-value <0.025).

[42] - 1-sided p-value

Statistical analysis title	Percentage Difference : Serotype 7F

Statistical analysis description:

Percentage difference (V114 minus Prevenar 13™), CI, and p-value are based on the Miettinen & Nurminen method.

Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	non-inferiority[43]
P-value	< 0.001 [44]
Method	Miettinen & Nurminen
Parameter estimate	Percentage Difference
Point estimate	0

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

Notes:

[43] - Non-inferiority of V114 to Prevenar 13™ is based on the lower bound of the 95% CI for the difference in percentages (V114 - Prevenar 13™) being >-10 percentage points (1-sided p-value <0.025).
[44] - 1-sided p-value

Statistical analysis title	Percentage Difference : Serotype 9V

Statistical analysis description:

Percentage difference (V114 minus Prevenar 13™), CI, and p-value are based on the Miettinen & Nurminen method.

Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	non-inferiority[45]
P-value	< 0.001 [46]
Method	Miettinen & Nurminen
Parameter estimate	Percentage Difference
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.4
upper limit	-0.4

Notes:

[45] - Non-inferiority of V114 to Prevenar 13™ is based on the lower bound of the 95% CI for the difference in percentages (V114 - Prevenar 13™) being >-10 percentage points (1-sided p-value <0.025).
[46] - 1-sided p-value

Statistical analysis title	Percentage Difference : Serotype 14

Statistical analysis description:

Percentage difference (V114 minus Prevenar 13™), CI, and p-value are based on the Miettinen & Nurminen method.

Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	non-inferiority[47]
P-value	< 0.001 [48]
Method	Miettinen & Nurminen
Parameter estimate	Percentage Difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	0.5

Notes:

[47] - Non-inferiority of V114 to Prevenar 13™ is based on the lower bound of the 95% CI for the difference in percentages (V114 - Prevenar 13™) being >-10 percentage points (1-sided p-value <0.025).

[48] - 1-sided p-value

Statistical analysis title	Percentage Difference : Serotype 18C
Statistical analysis description:	
Percentage difference (V114 minus Prevenar 13™), CI, and p-value are based on the Miettinen & Nurminen method.	
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	non-inferiority[49]
P-value	< 0.001 [50]
Method	Miettinen & Nurminen
Parameter estimate	Percentage Difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.8
upper limit	0.9

Notes:

[49] - Non-inferiority of V114 to Prevenar 13™ is based on the lower bound of the 95% CI for the difference in percentages (V114 - Prevenar 13™) being >-10 percentage points (1-sided p-value <0. 025).
[50] - 1-sided p-value

Statistical analysis title	Percentage Difference : Serotype 19A
Statistical analysis description:	
Percentage difference (V114 minus Prevenar 13™), CI, and p-value are based on the Miettinen & Nurminen method.	
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	non-inferiority[51]
P-value	< 0.001 [52]
Method	Miettinen & Nurminen
Parameter estimate	Percentage Difference
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.2
upper limit	-0.2

Notes:

[51] - Non-inferiority of V114 to Prevenar 13™ is based on the lower bound of the 95% CI for the difference in percentages (V114 - Prevenar 13™) being >-10 percentage points (1-sided p-value <0. 025).
[52] - 1-sided p-value

Statistical analysis title	Percentage Difference : Serotype 19F
Statistical analysis description:	
Percentage difference (V114 minus Prevenar 13™), CI, and p-value are based on the Miettinen & Nurminen method.	
Comparison groups	V114 v Prevenar 13™

Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	non-inferiority[53]
P-value	< 0.001 [54]
Method	Miettinen & Nurminen
Parameter estimate	Percentage Difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	0.3

Notes:

[53] - Non-inferiority of V114 to Prevenar 13™ is based on the lower bound of the 95% CI for the difference in percentages (V114 - Prevenar 13™) being >-10 percentage points (1-sided p-value <0.025).

[54] - 1-sided p-value

Statistical analysis title	Percentage Difference : Serotype 23F

Statistical analysis description:

Percentage difference (V114 minus Prevenar 13™), CI, and p-value are based on the Miettinen & Nurminen method.

Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	non-inferiority[55]
P-value	< 0.001 [56]
Method	Miettinen & Nurminen
Parameter estimate	Percentage Difference
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.7
upper limit	1.5

Notes:

[55] - Non-inferiority of V114 to Prevenar 13™ is based on the lower bound of the 95% CI for the difference in percentages (V114 - Prevenar 13™) being >-10 percentage points (1-sided p-value <0.025).

[56] - 1-sided p-value

Statistical analysis title	Percentage Difference : Serotype 22F

Statistical analysis description:

Percentage difference (V114 minus Prevenar 13™), CI, and p-value are based on the Miettinen & Nurminen method.

Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	superiority[57]
P-value	< 0.001 [58]
Method	Miettinen & Nurminen
Parameter estimate	Percentage Difference
Point estimate	93.8

Confidence interval	
level	95 %
sides	2-sided
lower limit	91.5
upper limit	95.6

Notes:

[57] - Superiority of V114 to Prevenar 13™ is based on the lower bound of the 95% CI for the difference in percentages (V114 - Prevenar 13™) being >10 percentage points (1-sided p-value <0.025).
[58] - 1-sided p-value

Statistical analysis title	Percentage Difference : Serotype 33F

Statistical analysis description:

Percentage difference (V114 minus Prevenar 13™), CI, and p-value are based on the Miettinen & Nurminen method.

Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	superiority[59]
P-value	< 0.001 [60]
Method	Miettinen & Nurminen
Parameter estimate	Percentage Difference
Point estimate	94.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	92.7
upper limit	96.5

Notes:

[59] - Superiority of V114 to Prevenar 13™ is based on the lower bound of the 95% CI for the difference in percentages (V114 - Prevenar 13™) being >10 percentage points (1-sided p-value <0.025).
[60] - 1-sided p-value

Secondary: Percentage of Participants Who Meet Antigen-Specific Threshold Value for Each Antigen in Infanrix™ Hexa at 30 Days PTD

End point title	Percentage of Participants Who Meet Antigen-Specific Threshold Value for Each Antigen in Infanrix™ Hexa at 30 Days PTD

End point description:

Sera from participants was used to measure vaccine-induced responses to 10 pre-specified Infanrix™ hexa antigens with the following threshold (% ≥) values: Diphtheria toxoid-0.1 international unit (IU)/mL;Tetanus toxoid-0.1 IU/mL; Pertussis pertussis toxin (PT)-5 endotoxin unit (EU)/mL; Pertussis filamentous hemagglutinin (FHA)-5 EU/mL; Pertussis pertactin (PRN)-5 EU/mL; Haemophilus influenzae type b (Hib) polyribosylribitol phosphate (PRP)-0.15 µg/mL; hepatitis B surface antigen (HBsAg)-10 mIU/mL; Poliovirus 1,2 and 3-1:8 neutralizing antibodies (NAb) dilution.The population analyzed consisted of all randomized participants without deviations from the protocol that may substantially affect the results, and had data available for each antigen.

End point type	Secondary

End point timeframe:

30 days PTD (Up to approximately study month 14)

End point values	V114	Prevenar 13™		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	588	591		
Units: Percentage of Participants				
number (not applicable)				
Diphtheria toxoid (n=537,533)	99.3	99.8		
Tetanus toxoid (n=537,533)	99.6	100.0		
Pertussis PT (n=537,533)	99.4	99.6		
Pertussis FHA (n=537,533)	99.8	100.0		
Pertussis PRN (n=537,533)	99.6	100.0		
Hib PRP (n=524,523)	98.5	98.1		
HBsAg (n=522,521)	99.2	100.0		
Poliovirus 1 (n=526,521)	100.0	100.0		
Poliovirus 2 (n=525,525)	100.0	100.0		
Poliovirus 3 (n=531,523)	100.0	99.8		

Statistical analyses

Statistical analysis title	Percentage Difference : Diphtheria toxoid

Statistical analysis description:

Percentage difference (V114 minus Prevenar 13™), CI, and p-value are based on the Miettinen & Nurminen method.

Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	non-inferiority[61]
P-value	< 0.001 [62]
Method	Miettinen & Nurminen
Parameter estimate	Percentage Difference
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.7
upper limit	0.4

Notes:

[61] - Non-inferiority of Infanrix™ hexa administered concomitantly with V114 to Infanrix™ hexa administered concomitantly with Prevenar 13™ is based on the lower bound of the 2-sided 95% CI for the difference in percentages (V114 - Prevenar 13™) being greater than the -10% specified non-inferiority margin (1-sided p-value <0.025).

[62] - 1-sided p-value

Statistical analysis title	Percentage Difference : Tetanus toxoid

Statistical analysis description:

Percentage difference (V114 minus Prevenar 13™), CI, and p-value are based on the Miettinen & Nurminen method.

Comparison groups	V114 v Prevenar 13™

Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	non-inferiority[63]
P-value	< 0.001 [64]
Method	Miettinen & Nurminen
Parameter estimate	Percentage Difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	0.3

Notes:

[63] - Non-inferiority of Infanrix™ hexa administered concomitantly with V114 to Infanrix™ hexa administered concomitantly with Prevenar 13™ is based on the lower bound of the 2-sided 95% CI for the difference in percentages (V114 - Prevenar 13™) being greater than the -5% specified non-inferiority margin (1-sided p-value <0.025).
[64] - 1-sided p-value

Statistical analysis title	Percentage Difference : Pertussis - PT

Statistical analysis description:

Percentage difference (V114 minus Prevenar 13™), CI, and p-value are based on the Miettinen & Nurminen method.

Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	non-inferiority[65]
P-value	< 0.001 [66]
Method	Miettinen & Nurminen
Parameter estimate	Percentage Difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	0.9

Notes:

[65] - Non-inferiority of Infanrix™ hexa administered concomitantly with V114 to Infanrix™ hexa administered concomitantly with Prevenar 13™ is based on the lower bound of the 2-sided 95% CI for the difference in percentages (V114 - Prevenar 13™) being greater than the -10% specified non-inferiority margin (1-sided p-value <0.025).
[66] - 1-sided p-value

Statistical analysis title	Percentage Difference : Pertussis - FHA

Statistical analysis description:

Percentage difference (V114 minus Prevenar 13™), CI, and p-value are based on the Miettinen & Nurminen method.

Comparison groups	V114 v Prevenar 13™

Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	non-inferiority[67]
P-value	< 0.001 [68]
Method	Miettinen & Nurminen
Parameter estimate	Percentage Difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	0.5

Notes:

[67] - Non-inferiority of Infanrix™ hexa administered concomitantly with V114 to Infanrix™ hexa administered concomitantly with Prevenar 13™ is based on the lower bound of the 2-sided 95% CI for the difference in percentages (V114 - Prevenar 13™) being greater than the -10% specified non-inferiority margin (1-sided p-value <0.025).
[68] - 1-sided p-value

Statistical analysis title	Percentage Difference : Pertussis - PRN

Statistical analysis description:

Percentage difference (V114 minus Prevenar 13™), CI, and p-value are based on the Miettinen & Nurminen method.

Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	non-inferiority[69]
P-value	< 0.001 [70]
Method	Miettinen & Nurminen
Parameter estimate	Percentage Difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	0.3

Notes:

[69] - Non-inferiority of Infanrix™ hexa administered concomitantly with V114 to Infanrix™ hexa administered concomitantly with Prevenar 13™ is based on the lower bound of the 2-sided 95% CI for the difference in percentages (V114 - Prevenar 13™) being greater than the -10% specified non-inferiority margin (1-sided p-value <0.025).
[70] - 1-sided p-value

Statistical analysis title	Percentage Difference : Hib-PRP

Statistical analysis description:

Percentage difference (V114 minus Prevenar 13™), CI, and p-value are based on the Miettinen & Nurminen method.

Comparison groups	V114 v Prevenar 13™

Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	non-inferiority[71]
P-value	< 0.001 [72]
Method	Miettinen & Nurminen
Parameter estimate	Percentage Difference
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	2.1

Notes:

[71] - Non-inferiority of Infanrix™ hexa administered concomitantly with V114 to Infanrix™ hexa administered concomitantly with Prevenar 13™ is based on the lower bound of the 2-sided 95% CI for the difference in percentages (V114 - Prevenar 13™) being greater than the -10% specified non-inferiority margin (1-sided p-value <0.025).
[72] - 1-sided p-value

Statistical analysis title	Percentage Difference : HBsAg

Statistical analysis description:

Percentage difference (V114 minus Prevenar 13™), CI, and p-value are based on the Miettinen & Nurminen method.

Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	non-inferiority[73]
P-value	< 0.001 [74]
Method	Miettinen & Nurminen
Parameter estimate	Percentage Difference
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	0

Notes:

[73] - Non-inferiority of Infanrix™ hexa administered concomitantly with V114 to Infanrix™ hexa administered concomitantly with Prevenar 13™ is based on the lower bound of the 2-sided 95% CI for the difference in percentages (V114 - Prevenar 13™) being greater than the -10% specified non-inferiority margin (1-sided p-value <0.025).
[74] - 1-sided p-value

Statistical analysis title	Percentage Difference : Poliovirus 1

Statistical analysis description:

Percentage difference (V114 minus Prevenar 13™), CI, and p-value are based on the Miettinen & Nurminen method.

Comparison groups	V114 v Prevenar 13™

Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	non-inferiority[75]
P-value	< 0.001 [76]
Method	Miettinen & Nurminen
Parameter estimate	Percentage Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	0.7

Notes:

[75] - Non-inferiority of Infanrix™ hexa administered concomitantly with V114 to Infanrix™ hexa administered concomitantly with Prevenar 13™ is based on the lower bound of the 2-sided 95% CI for the difference in percentages (V114 - Prevenar 13™) being greater than the -5% specified non-inferiority margin (1-sided p-value <0.025).
[76] - 1-sided p-value

Statistical analysis title	Percentage Difference : Poliovirus 2

Statistical analysis description:

Percentage difference (V114 minus Prevenar 13™), CI, and p-value are based on the Miettinen & Nurminen method.

Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	non-inferiority[77]
P-value	< 0.001 [78]
Method	Miettinen & Nurminen
Parameter estimate	Percentage Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	0.7

Notes:

[77] - Non-inferiority of Infanrix™ hexa administered concomitantly with V114 to Infanrix™ hexa administered concomitantly with Prevenar 13™ is based on the lower bound of the 2-sided 95% CI for the difference in percentages (V114 - Prevenar 13™) being greater than the -5% specified non-inferiority margin (1-sided p-value <0.025).
[78] - 1-sided p-value

Statistical analysis title	Percentage Difference : Poliovirus 3

Statistical analysis description:

Percentage difference (V114 minus Prevenar 13™), CI, and p-value are based on the Miettinen & Nurminen method.

Comparison groups	V114 v Prevenar 13™

Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	non-inferiority[79]
P-value	< 0.001 [80]
Method	Miettinen & Nurminen
Parameter estimate	Percentage Difference
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	1.1

Notes:

[79] - Non-inferiority of Infanrix™ hexa administered concomitantly with V114 to Infanrix™ hexa administered concomitantly with Prevenar 13™ is based on the lower bound of the 2-sided 95% CI for the difference in percentages (V114 - Prevenar 13™) being greater than the -5% specified non-inferiority margin (1-sided p-value <0.025).

[80] - 1-sided p-value

Secondary: Anti-rotavirus Immunoglobulin A (IgA) Geometric Mean Titers (GMTs) of Rotarix™ at 30 Days Post Primary Series (PPS)

End point title	Anti-rotavirus Immunoglobulin A (IgA) Geometric Mean Titers (GMTs) of Rotarix™ at 30 Days Post Primary Series (PPS)

End point description:

Sera from participants was used to measure vaccine-induced antibodies in response to vaccination with Rotarix™ by assessing the GMT for IgA. The population analyzed consisted of all randomized participants without deviations from the protocol that may substantially affect the results. Deviations that affect the number analyzed include, but are not limited to, failure to receive vaccination; receipt of prohibited medication or vaccine; failure to receive vaccination at the required time point; failure to receive the required vaccination dose; and collection of blood sample at a time point outside of the prespecified time window.

End point type	Secondary

End point timeframe:

30 days PPS (Up to approximately study month 3)

End point values	V114	Prevenar 13™		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	520	503		
Units: Titer				
number (not applicable)	45.39	47.07		

Statistical analyses

Statistical analysis title	GMT Ratio

Statistical analysis description:

GMT ratio (V114/Prevenar 13™), CI, and p-value are calculated using the t-distribution with the variance estimate from a serotype-specific linear model utilizing the natural log-transformed antibody concentrations as the response and a single term for
vaccination group

Comparison groups	V114 v Prevenar 13™

Number of subjects included in analysis	1023
Analysis specification	Pre-specified
Analysis type	non-inferiority[81]
P-value	< 0.001 [82]
Method	t-distribution
Parameter estimate	GMT Ratio
Point estimate	0.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8
upper limit	1.16

Notes:

[81] - Non-inferiority of Rotarix™ administered concomitantly with V114 to Rotarix™ administered concomitantly with Prevenar 13™ is based on the lower bound of the 2-sided 95% CI for the GMT ratio (V114/Prevenar 13™) being >0.5 (1-sided p-value <0.025).

[82] - 1-sided p-value

Secondary: Anti-PnPs Serotype-specific IgG GMCs for Each Serotype at 30 Days PPS

End point title	Anti-PnPs Serotype-specific IgG GMCs for Each Serotype at 30 Days PPS

End point description:

Sera from participants was used to measure vaccine-induced anti-PnPs serotype-specific IgG for each serotype using PnECL. The GMC for each of the 13 serotypes shared by both V114 and Prevenar 13™ (Serotypes 1 to 23F); and the 2 serotypes unique to V114 (Serotypes 22F and 33F) was assessed. The population analyzed consisted of all randomized participants without deviations from the protocol that may substantially affect the results. Deviations that affect the number analyzed include, but are not limited to, failure to receive vaccination; receipt of prohibited medication or vaccine; failure to receive vaccination at the required time point; failure to receive the required vaccination dose; and collection of blood sample at a time point outside of the prespecified time window.

End point type	Secondary

End point timeframe:

30 days PPS (Up to approximately study month 3)

End point values	V114	Prevenar 13™		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	588	591		
Units: µg/mL				
number (not applicable)				
Serotype 1 (n=522,500)	1.30	1.62		
Serotype 3 (n=522,500)	0.88	0.48		
Serotype 4 (n=522,500)	1.41	1.30		
Serotype 5 (n=522,500)	0.89	1.06		
Serotype 6A (n=522,500)	0.64	1.42		
Serotype 6B (n=522,499)	0.43	0.36		
Serotype 7F (n=522,500)	2.04	2.46		
Serotype 9V (n=522,500)	1.23	1.43		
Serotype 14 (n=522,500)	3.87	5.14		
Serotype 18C (n=522,500)	1.17	1.37		
Serotype 19A (n=522,500)	1.71	2.20		
Serotype 19F (n=522,500)	2.63	3.40		
Serotype 23F (n=522,499)	0.76	0.62		

Serotype 22F (n=522,500)	2.76	0.05		
Serotype 33F(n=522,500)	0.31	0.05		

Statistical analyses

Statistical analysis title	GMC Ratio : Serotype 1
Statistical analysis description:	
GMC ratio (V114 / Prevenar 13™) and CI are calculated using the t-distribution with the variance estimate from a serotype-specific linear model utilizing the natural log-transformed antibody concentrations as the response and a single term for vaccination group.	
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC Ratio
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.73
upper limit	0.88

Statistical analysis title	GMC Ratio : Serotype 3
Statistical analysis description:	
GMC ratio (V114 / Prevenar 13™) and CI are calculated using the t-distribution with the variance estimate from a serotype-specific linear model utilizing the natural log-transformed antibody concentrations as the response and a single term for vaccination group.	
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC Ratio
Point estimate	1.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.7
upper limit	2.02

Statistical analysis title	GMC Ratio : Serotype 4
Statistical analysis description:	
GMC ratio (V114 / Prevenar 13™) and CI are calculated using the t-distribution with the variance estimate from a serotype-specific linear model utilizing the natural log-transformed antibody concentrations as the response and a single term for vaccination group.	
Comparison groups	V114 v Prevenar 13™

Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC Ratio
Point estimate	1.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.98
upper limit	1.19

Statistical analysis title	GMC Ratio : Serotype 5

Statistical analysis description:

GMC ratio (V114 / Prevenar 13™) and CI are calculated using the t-distribution with the variance estimate from a serotype-specific linear model utilizing the natural log-transformed antibody concentrations as the response and a single term for vaccination group.

Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC Ratio
Point estimate	0.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.74
upper limit	0.94

Statistical analysis title	GMC Ratio : Serotype 6A

Statistical analysis description:

GMC ratio (V114 / Prevenar 13™) and CI are calculated using the t-distribution with the variance estimate from a serotype-specific linear model utilizing the natural log-transformed antibody concentrations as the response and a single term for vaccination group.

Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC Ratio
Point estimate	0.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.4
upper limit	0.52

Statistical analysis title	GMC Ratio : Serotype 6B
Statistical analysis description:	
GMC ratio (V114 / Prevenar 13™) and CI are calculated using the t-distribution with the variance estimate from a serotype-specific linear model utilizing the natural log-transformed antibody concentrations as the response and a single term for vaccination group.	
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC Ratio
Point estimate	1.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	1
upper limit	1.41

Statistical analysis title	GMC Ratio : Serotype 7F
Statistical analysis description:	
GMC ratio (V114 / Prevenar 13™) and CI are calculated using the t-distribution with the variance estimate from a serotype-specific linear model utilizing the natural log-transformed antibody concentrations as the response and a single term for vaccination group.	
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC Ratio
Point estimate	0.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.76
upper limit	0.91

Statistical analysis title	GMC Ratio : Serotype 14
Statistical analysis description:	
GMC ratio (V114 / Prevenar 13™) and CI are calculated using the t-distribution with the variance estimate from a serotype-specific linear model utilizing the natural log-transformed antibody concentrations as the response and a single term for vaccination group.	
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC Ratio
Point estimate	0.75

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.66
upper limit	0.86

Statistical analysis title	GMC Ratio : Serotype 9V

Statistical analysis description:

GMC ratio (V114 / Prevenar 13™) and CI are calculated using the t-distribution with the variance estimate from a serotype-specific linear model utilizing the natural log-transformed antibody concentrations as the response and a single term for vaccination group.

Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC Ratio
Point estimate	0.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.77
upper limit	0.96

Statistical analysis title	GMC Ratio : Serotype 18C

Statistical analysis description:

GMC ratio (V114 / Prevenar 13™) and CI are calculated using the t-distribution with the variance estimate from a serotype-specific linear model utilizing the natural log-transformed antibody concentrations as the response and a single term for vaccination group.

Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC Ratio
Point estimate	0.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.77
upper limit	0.95

Statistical analysis title	GMC Ratio : Serotype 19A

Statistical analysis description:

GMC ratio (V114 / Prevenar 13™) and CI are calculated using the t-distribution with the variance estimate from a serotype-specific linear model utilizing the natural log-transformed antibody concentrations as the response and a single term for vaccination group.

Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC Ratio
Point estimate	0.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	0.87

Statistical analysis title	GMC Ratio : Serotype 19F

Statistical analysis description:

GMC ratio (V114 / Prevenar 13™) and CI are calculated using the t-distribution with the variance estimate from a serotype-specific linear model utilizing the natural log-transformed antibody concentrations as the response and a single term for vaccination group.

Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC Ratio
Point estimate	0.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	0.85

Statistical analysis title	GMC Ratio : Serotype 23F

Statistical analysis description:

GMC ratio (V114 / Prevenar 13™) and CI are calculated using the t-distribution with the variance estimate from a serotype-specific linear model utilizing the natural log-transformed antibody concentrations as the response and a single term for vaccination group.

Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC Ratio
Point estimate	1.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.07
upper limit	1.4

Statistical analysis title	GMC Ratio : Serotype 22F

Statistical analysis description:

GMC ratio (V114 / Prevenar 13™) and CI are calculated using the t-distribution with the variance estimate from a serotype-specific linear model utilizing the natural log-transformed antibody concentrations as the response and a single term for vaccination group.

Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC Ratio
Point estimate	57.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	51.2
upper limit	65

Statistical analysis title	GMC Ratio : Serotype 33F

Statistical analysis description:

GMC ratio (V114 / Prevenar 13™) and CI are calculated using the t-distribution with the variance estimate from a serotype-specific linear model utilizing the natural log-transformed antibody concentrations as the response and a single term for vaccination group.

Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMC Ratio
Point estimate	6.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.46
upper limit	7.14

Secondary: Percentage of Participants Who Meet Serotype-specific IgG Threshold Value of ≥0.35 µg/mL for Each Serotype at 30 Days PPS

End point title	Percentage of Participants Who Meet Serotype-specific IgG Threshold Value of ≥0.35 µg/mL for Each Serotype at 30 Days PPS

End point description:

Sera from participants was used to measure vaccine-induced anti-PnPs serotype-specific IgG for the 15 serotypes using PnECL. The percentage of participants that achieve the threshold value of ≥0.35 µg/mL for each of the 13 serotypes shared by both V114 and Prevenar 13™ (Serotypes 1 to 23F); and the 2 serotypes unique to V114 (Serotypes 22F and 33F) was assessed. The population analyzed consisted of all randomized participants without deviations from the protocol that may substantially affect the results. Deviations that affect the number analyzed include, but are not limited to, failure to receive

vaccination; receipt of prohibited medication or vaccine; failure to receive vaccination at the required time point; failure to receive the required vaccination dose; and collection of blood sample at a time point outside of the prespecified time window.

End point type	Secondary

End point timeframe:

30 days PPS (Up to approximately study month 3)

End point values	V114	Prevenar 13™		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	588	591		
Units: Percentage of Participants				
number (not applicable)				
Serotype 1 (n=522,500)	95.4	97.4		
Serotype 3 (n=522,500)	93.5	67.8		
Serotype 4 (n=522,500)	93.9	96.8		
Serotype 5 (n=522,500)	84.5	88.4		
Serotype 6A (n=522,500)	73.2	92.6		
Serotype 6B (n=522,499)	57.3	52.7		
Serotype 7F (n=522,500)	97.9	99.0		
Serotype 9V (n=522,500)	88.7	95.4		
Serotype 14 (n=522,500)	96.9	97.4		
Serotype 18C (n=522,500)	92.3	93.0		
Serotype 19A (n=522,500)	96.2	97.4		
Serotype 19F (n=522,500)	98.9	99.4		
Serotype 23F (n=522,499)	78.5	71.9		
Serotype 22F(n=522,500)	95.6	5.2		
Serotype 33F (n=522,500)	48.7	2.8		

Statistical analyses

Statistical analysis title	Percentage Difference : Serotype 1

Statistical analysis description:

Percentage difference (V114 minus Prevenar 13™) and CI are based on the Miettinen & Nurminen method.

Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Percentage Difference
Point estimate	-2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.4
upper limit	0.3

Statistical analysis title	Percentage Difference : Serotype 3
Statistical analysis description: Percentage difference (V114 minus Prevenar 13™) and CI are based on the Miettinen & Nurminen method.	
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Percentage Difference
Point estimate	25.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	21.1
upper limit	30.3

Statistical analysis title	Percentage Difference : Serotype 4
Statistical analysis description: Percentage difference (V114 minus Prevenar 13™) and CI are based on the Miettinen & Nurminen method.	
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Percentage Difference
Point estimate	-2.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.7
upper limit	-0.3

Statistical analysis title	Percentage Difference : Serotype 5
Statistical analysis description: Percentage difference (V114 minus Prevenar 13™) and CI are based on the Miettinen & Nurminen method.	
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Percentage Difference
Point estimate	-3.9

Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.1
upper limit	0.3

Statistical analysis title	Percentage Difference : Serotype 6A
Statistical analysis description:	
Percentage difference (V114 minus Prevenar 13™) and CI are based on the Miettinen & Nurminen method.	
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Percentage Difference
Point estimate	-19.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-23.9
upper limit	-15

Statistical analysis title	Percentage Difference : Serotype 6B
Statistical analysis description:	
Percentage difference (V114 minus Prevenar 13™) and CI are based on the Miettinen & Nurminen method.	
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Percentage Difference
Point estimate	4.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	10.7

Statistical analysis title	Percentage Difference : Serotype 7F
Statistical analysis description:	
Percentage difference (V114 minus Prevenar 13™) and CI are based on the Miettinen & Nurminen method.	
Comparison groups	V114 v Prevenar 13™

Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Percentage Difference
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.9
upper limit	0.5

Statistical analysis title	Percentage Difference : Serotype 9V
Statistical analysis description:	
Percentage difference (V114 minus Prevenar 13™) and CI are based on the Miettinen & Nurminen method.	
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Percentage Difference
Point estimate	-6.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.1
upper limit	-3.5

Statistical analysis title	Percentage Difference : Serotype 14
Statistical analysis description:	
Percentage difference (V114 minus Prevenar 13™) and CI are based on the Miettinen & Nurminen method.	
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Percentage Difference
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.6
upper limit	1.7

Statistical analysis title	Percentage Difference : Serotype 18C

Statistical analysis description:

Percentage difference (V114 minus Prevenar 13™) and CI are based on the Miettinen & Nurminen method.

Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Percentage Difference
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.9
upper limit	2.6

Statistical analysis title	Percentage Difference : Serotype 19A

Statistical analysis description:

Percentage difference (V114 minus Prevenar 13™) and CI are based on the Miettinen & Nurminen method.

Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Percentage Difference
Point estimate	-1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.5
upper limit	1

Statistical analysis title	Percentage Difference : Serotype 19F

Statistical analysis description:

Percentage difference (V114 minus Prevenar 13™) and CI are based on the Miettinen & Nurminen method.

Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Percentage Difference
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	0.7

Statistical analysis title	Percentage Difference : Serotype 23F
Statistical analysis description: Percentage difference (V114 minus Prevenar 13™) and CI are based on the Miettinen & Nurminen method.	
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Percentage Difference
Point estimate	6.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.3
upper limit	11.9

Statistical analysis title	Percentage Difference : Serotype 22F
Statistical analysis description: Percentage difference (V114 minus Prevenar 13™) and CI are based on the Miettinen & Nurminen method.	
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Percentage Difference
Point estimate	90.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	87.4
upper limit	92.7

Statistical analysis title	Percentage Difference : Serotype 33F
Statistical analysis description: Percentage difference (V114 minus Prevenar 13™) and CI are based on the Miettinen & Nurminen method.	
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Percentage Difference
Point estimate	45.9

Confidence interval	
level	95 %
sides	2-sided
lower limit	41.3
upper limit	50.3

Secondary: Anti-PnPs Serotype-specific Opsonophagocytic Activity (OPA) GMTs for Each Serotype at 30 Days PTD

End point title	Anti-PnPs Serotype-specific Opsonophagocytic Activity (OPA) GMTs for Each Serotype at 30 Days PTD

End point description:

Sera from participants was used to measure vaccine-induced anti-PnPs serotype-specific OPA using the multiplexed opsonophagocytic assay (MOPA). The GMT for each of the 13 serotypes shared by both V114 and Prevenar 13™ (Serotypes 1 to 23F); and the 2 serotypes unique to V114 (Serotypes 22F and 33F) was assessed. The within-group CIs were obtained by exponentiating the CIs of the mean of the natural log values based on the t-distribution. The population analyzed consists of all randomized participants without deviations from the protocol that may substantially affect the results. Deviations that affect the number analyzed include, but are not limited to, failure to receive vaccination; receipt of prohibited medication or vaccine; failure to receive vaccination at the required time point; failure to receive the required vaccination dose; and collection of blood sample at a time point outside of the prespecified time window.

End point type	Secondary

End point timeframe:

30 days PTD (Up to approximately study month 14)

End point values	V114	Prevenar 13™		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	116	122		
Units: Titer				
geometric mean (confidence interval 95%)				
Serotype 1 (n=101,108)	136.8 (107.2 to 174.6)	164.6 (127.9 to 211.8)		
Serotype 3 (n=98,103)	321.5 (277.2 to 372.9)	303.0 (253.2 to 362.6)		
Serotype 4 (n=97,99)	2231.7 (1770.5 to 2813.1)	3206.4 (2626.6 to 3914.1)		
Serotype 5 (n=102,108)	791.6 (640.9 to 977.8)	947.9 (784.3 to 1145.7)		
Serotype 6A (n=98,99)	3274.9 (2734.5 to 3921.9)	5387.2 (4388.9 to 6612.5)		
Serotype 6B (n=94,95)	2439.9 (1936.1 to 3074.7)	3182.4 (2500.9 to 4049.7)		
Serotype 7F (n=97,100)	6300.9 (5363.9 to 7401.7)	10071.4 (8327.2 to 12181.0)		
Serotype 9V (n=97,103)	1904.4 (1584.8 to 2288.4)	2616.6 (2133.3 to 3209.4)		

Serotype 14 (n=99,100)	2633.8 (2102.6 to 3299.2)	2582.1 (2089.5 to 3190.9)		
Serotype 18C (n=98,103)	1968.6 (1676.4 to 2311.7)	2091.8 (1789.1 to 2445.7)		
Serotype 19A (n=101,104)	2995.6 (2556.5 to 3510.0)	4254.3 (3649.3 to 4959.5)		
Serotype 19F (n=98,103)	1793.9 (1535.3 to 2096.1)	2012.3 (1677.0 to 2414.6)		
Serotype 23F (n=97,99)	4517.8 (3685.1 to 5538.8)	7987.6 (6149.3 to 10375.5)		
Serotype 22F (n=98,96)	2405.2 (1980.5 to 2921.0)	24.5 (16.0 to 37.7)		
Serotype 33F (n=96,101)	14268.4 (11680.1 to 17430.2)	1875.6 (1477.4 to 2381.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Meet Serotype-specific OPA Threshold Value for Each Serotype at 30 Days PTD

End point title	Percentage of Participants Who Meet Serotype-specific OPA Threshold Value for Each Serotype at 30 Days PTD

End point description:

Sera from participants was used to measure vaccine-induced anti-PnPs serotype-specific OPA using the MOPA. The threshold dilution (% ≥) for each of the 13 serotypes shared by both V114 and Prevenar 13™ (Serotypes 1 to 23F) were as follows: 1:9, 1:19, 1:34, 1:27, 1:232, 1:40, 1:61, 1:151, 1:62, 1:115, 1:31, 1:113, 1:55. For Serotypes 22F and 33F the threshold dilution was 1:15 and 1:20 respectively. The within-group CIs were based on the exact binomial method of Clopper and Pearson. The population analyzed consisted of all randomized participants without deviations from the protocol that may substantially affect the results. Deviations that affect the number analyzed include, but are not limited to, failure to receive vaccination; receipt of prohibited medication or vaccine; failure to receive vaccination at the required time point; failure to receive the required vaccination dose; and collection of blood sample at a time point outside of the prespecified time window.

End point type	Secondary

End point timeframe:

30 days PTD (Up to approximately study month 14)

End point values	V114	Prevenar 13™		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	116	122		
Units: Percentage of Participants				
number (confidence interval 95%)				
Serotype 1 (n=101,108)	95.0 (88.8 to 98.4)	98.1 (93.5 to 99.8)		
Serotype 3 (n=98,103)	100.0 (96.3 to 100.0)	98.1 (93.2 to 99.8)		

Serotype 4 (n=97,99)	100.0 (96.3 to 100.0)	100.0 (96.3 to 100.0)		
Serotype 5 (n=102,108)	100.0 (96.4 to 100.0)	100.0 (96.6 to 100.0)		
Serotype 6A (n=98,99)	99.0 (94.4 to 100.0)	100.0 (96.3 to 100.0)		
Serotype 6B (n=94,95)	100.0 (96.2 to 100.0)	100.0 (96.2 to 100.0)		
Serotype 7F (n=97,100)	100.0 (96.3 to 100.0)	100.0 (96.4 to 100.0)		
Serotype 9V (n=97,103)	97.9 (92.7 to 99.7)	100.0 (96.5 to 100.0)		
Serotype 14 (n=99,100)	100.0 (96.3 to 100.0)	99.0 (94.6 to 100.0)		
Serotype 18C (n=98,103)	100.0 (96.3 to 100.0)	100.0 (96.5 to 100.0)		
Serotype 19A (n=101,104)	100.0 (96.4 to 100.0)	100.0 (96.5 to 100.0)		
Serotype 19F (n=98,103)	100.0 (96.3 to 100.0)	99.0 (94.7 to 100.0)		
Serotype 23F (n=97,99)	100.0 (96.3 to 100.0)	100.0 (96.3 to 100.0)		
Serotype 22F (n=98,96)	99.0 (94.4 to 100.0)	28.1 (19.4 to 38.2)		
Serotype 33F (n=96,101)	100.0 (96.2 to 100.0)	98.0 (93.0 to 99.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants for Serotypes 22F and 33F randomized to V114 compared with Serotype 3 randomized to Prevenar 13™ at 30 Days PTD

End point title	Percentage of Participants for Serotypes 22F and 33F randomized to V114 compared with Serotype 3 randomized to Prevenar 13™ at 30 Days PTD

End point description:

Sera from participants was used to measure vaccine-induced anti-PnPs serotype-specific IgG for the 15 serotypes using PnECL. As a protocol-specified endpoint the percentage of participants that achieve the threshold value of ≥0.35 µg/mL for Serotype 3, the serotype shared by both V114 and Prevenar 13™ that exhibits the lowest IgG response rate for Prevenar 13™, was compared to that of the 2 serotypes unique to V114 (Serotypes 22F and 33F). The population analyzed consisted of all randomized participants without deviations from the protocol that may substantially affect the results. Deviations that affect the number analyzed include, but are not limited to, failure to receive vaccination; receipt of prohibited medication or vaccine; failure to receive vaccination at the required time point; failure to receive the required vaccination dose; and collection of blood sample at a time point outside of the prespecified time window.

End point type	Secondary

End point timeframe:

30 days PTD (Up to approximately study month 14)

End point values	V114	Prevenar 13™		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	588[83]	591[84]		
Units: Percentage of Participants				
number (not applicable)				
Serotype 22F (n=539), Serotype 3 (n=537)	99.6	83.8		
Serotype 33F (n=539), Serotype 3 (n=537)	99.1	83.8		

Notes:

[83] - V114 Serotypes 22F, 33F

[84] - Prevenar 13™ Serotype 3

Statistical analyses

Statistical analysis title	Percentage Diff.: V114-33F minus Prevenar 13™-3
Statistical analysis description:	
Percentage difference and CI are based on the Miettinen & Nurminen method.	
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Percentage Difference
Point estimate	15.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	12.2
upper limit	18.7

Statistical analysis title	Percentage Diff.: V114-22F minus Prevenar 13™-3
Statistical analysis description:	
Percentage difference and CI are based on the Miettinen & Nurminen method.	
Comparison groups	V114 v Prevenar 13™
Number of subjects included in analysis	1179
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Percentage Difference
Point estimate	15.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	12.9
upper limit	19.2

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Non-serious AEs reported from Day 1 through 14 days following each vaccination. Serious AEs reported from Day 1 up to approximately study month 20. All-cause mortality (ACM) reported from randomization up to approximately study month 20.

Adverse event reporting additional description:

The ACM population was all randomized participants. For AEs the population was APaT, which consisted of participants who received at least 1 dose of study vaccination. The ACM and AEs for participants inadvertently vaccinated with both V114 and Prevenar 13™were reported separately from other participants.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	V114

Reporting group description:

Full-term infants received a 0.5 mL intramuscular injection of V114 at approximately 2, 4, and 11-15 months of age (Study Day 1, Month 2, and Month 9-13). Preterm infants received a 0.5 mL intramuscular injection of V114 at approximately 2, 3, 4,and 11-15 months of age (Study Day 1, Month 1, Month 2, and Month 9-13). All infants also received licensed background intramuscular injections of 0.5 mL Infanrix™ hexa at approximately 2, 3, 4, and 11-15 months of age (Study Day 1, Months 1, 2, and Month 9-13); and also 1.5 mL oral dose of Rotarix™ at 2 and 4 months of age (Study Day 1 and Month 2).

Reporting group title	V114 + Prevenar 13™

Reporting group description:

Participants inadvertently vaccinated with both V114 and Prevenar 13™

Reporting group title	Prevenar 13™

Reporting group description:

Full-term infants received a 0.5 mL intramuscular injection of Prevenar 13™ at approximately 2, 4, and 11-15 months of age (Study Day 1, Month 2, and Month 9-13). Preterm infants received a 0.5 mL intramuscular injection of Prevenar 13™ at approximately 2, 3, 4, and 11-15 months of age (Study Day 1, Month 1, Month 2, and Month 9-13). All infants also received licensed background intramuscular injections of 0.5 mL Infanrix™ hexa at approximately 2, 3, 4, and 11-15 months of age (Study Day 1, Months 1, 2, and Month 9-13); and also 1.5 mL oral dose of Rotarix™ at 2 and 4 months of age (Study Day 1 and Month 2).

Serious adverse events	V114	V114 + Prevenar 13™	Prevenar 13™
Total subjects affected by serious adverse events			
subjects affected / exposed	57 / 587 (9.71%)	0 / 1 (0.00%)	70 / 591 (11.84%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
General disorders and administration site conditions			
Influenza like illness			

subjects affected / exposed	0 / 587 (0.00%)	0 / 1 (0.00%)	2 / 591 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	1 / 587 (0.17%)	0 / 1 (0.00%)	1 / 591 (0.17%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Food allergy			
subjects affected / exposed	1 / 587 (0.17%)	0 / 1 (0.00%)	0 / 591 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypersensitivity			
subjects affected / exposed	0 / 587 (0.00%)	0 / 1 (0.00%)	1 / 591 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Bronchial hyperreactivity			
subjects affected / exposed	1 / 587 (0.17%)	0 / 1 (0.00%)	0 / 591 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Interstitial lung disease			
subjects affected / exposed	1 / 587 (0.17%)	0 / 1 (0.00%)	0 / 591 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Sleep disorder			
subjects affected / exposed	1 / 587 (0.17%)	0 / 1 (0.00%)	0 / 591 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Weight increased			

subjects affected / exposed	0 / 587 (0.00%)	0 / 1 (0.00%)	1 / 591 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Concussion			
subjects affected / exposed	1 / 587 (0.17%)	0 / 1 (0.00%)	2 / 591 (0.34%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foreign body ingestion			
subjects affected / exposed	0 / 587 (0.00%)	0 / 1 (0.00%)	1 / 591 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Contusion			
subjects affected / exposed	0 / 587 (0.00%)	0 / 1 (0.00%)	1 / 591 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Head injury			
subjects affected / exposed	0 / 587 (0.00%)	0 / 1 (0.00%)	1 / 591 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple fractures			
subjects affected / exposed	1 / 587 (0.17%)	0 / 1 (0.00%)	0 / 591 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thermal burn			
subjects affected / exposed	1 / 587 (0.17%)	0 / 1 (0.00%)	0 / 591 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Soft tissue injury			
subjects affected / exposed	0 / 587 (0.00%)	0 / 1 (0.00%)	1 / 591 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tooth injury			

subjects affected / exposed	1 / 587 (0.17%)	0 / 1 (0.00%)	0 / 591 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Epilepsy			
subjects affected / exposed	0 / 587 (0.00%)	0 / 1 (0.00%)	1 / 591 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile convulsion			
subjects affected / exposed	0 / 587 (0.00%)	0 / 1 (0.00%)	2 / 591 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infantile spasms			
subjects affected / exposed	0 / 587 (0.00%)	0 / 1 (0.00%)	1 / 591 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	0 / 587 (0.00%)	0 / 1 (0.00%)	1 / 591 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Haemolytic uraemic syndrome			
subjects affected / exposed	0 / 587 (0.00%)	0 / 1 (0.00%)	1 / 591 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Enterocolitis			
subjects affected / exposed	0 / 587 (0.00%)	0 / 1 (0.00%)	1 / 591 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	0 / 587 (0.00%)	0 / 1 (0.00%)	1 / 591 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 587 (0.00%)	0 / 1 (0.00%)	1 / 591 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal inflammation			
subjects affected / exposed	1 / 587 (0.17%)	0 / 1 (0.00%)	0 / 591 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	1 / 587 (0.17%)	0 / 1 (0.00%)	0 / 591 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Incarcerated inguinal hernia			
subjects affected / exposed	0 / 587 (0.00%)	0 / 1 (0.00%)	1 / 591 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			
subjects affected / exposed	0 / 587 (0.00%)	0 / 1 (0.00%)	1 / 591 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	0 / 587 (0.00%)	0 / 1 (0.00%)	1 / 591 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	1 / 587 (0.17%)	0 / 1 (0.00%)	1 / 591 (0.17%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Dermatitis atopic			
subjects affected / exposed	1 / 587 (0.17%)	0 / 1 (0.00%)	0 / 591 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue			

disorders			
Muscle spasms			
subjects affected / exposed	0 / 587 (0.00%)	0 / 1 (0.00%)	1 / 591 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bronchiolitis			
subjects affected / exposed	9 / 587 (1.53%)	0 / 1 (0.00%)	10 / 591 (1.69%)
occurrences causally related to treatment / all	0 / 11	0 / 0	0 / 10
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adenovirus infection			
subjects affected / exposed	0 / 587 (0.00%)	0 / 1 (0.00%)	1 / 591 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	1 / 587 (0.17%)	0 / 1 (0.00%)	3 / 591 (0.51%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis viral			
subjects affected / exposed	0 / 587 (0.00%)	0 / 1 (0.00%)	2 / 591 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Campylobacter gastroenteritis			
subjects affected / exposed	0 / 587 (0.00%)	0 / 1 (0.00%)	1 / 591 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia pyelonephritis			
subjects affected / exposed	0 / 587 (0.00%)	0 / 1 (0.00%)	2 / 591 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Exanthema subitum			
subjects affected / exposed	3 / 587 (0.51%)	0 / 1 (0.00%)	1 / 591 (0.17%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Gastritis viral			
subjects affected / exposed	1 / 587 (0.17%)	0 / 1 (0.00%)	0 / 591 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	3 / 587 (0.51%)	0 / 1 (0.00%)	8 / 591 (1.35%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 8
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis adenovirus			
subjects affected / exposed	1 / 587 (0.17%)	0 / 1 (0.00%)	2 / 591 (0.34%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis rotavirus			
subjects affected / exposed	0 / 587 (0.00%)	0 / 1 (0.00%)	1 / 591 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis sapovirus			
subjects affected / exposed	0 / 587 (0.00%)	0 / 1 (0.00%)	1 / 591 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngitis			
subjects affected / exposed	1 / 587 (0.17%)	0 / 1 (0.00%)	0 / 591 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	1 / 587 (0.17%)	0 / 1 (0.00%)	2 / 591 (0.34%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis viral			
subjects affected / exposed	0 / 587 (0.00%)	0 / 1 (0.00%)	1 / 591 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nasopharyngitis			

subjects affected / exposed	1 / 587 (0.17%)	0 / 1 (0.00%)	0 / 591 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media			
subjects affected / exposed	2 / 587 (0.34%)	0 / 1 (0.00%)	3 / 591 (0.51%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oral herpes			
subjects affected / exposed	1 / 587 (0.17%)	0 / 1 (0.00%)	0 / 591 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media acute			
subjects affected / exposed	2 / 587 (0.34%)	0 / 1 (0.00%)	1 / 591 (0.17%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media chronic			
subjects affected / exposed	2 / 587 (0.34%)	0 / 1 (0.00%)	0 / 591 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Periorbital cellulitis			
subjects affected / exposed	0 / 587 (0.00%)	0 / 1 (0.00%)	1 / 591 (0.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngitis			
subjects affected / exposed	1 / 587 (0.17%)	0 / 1 (0.00%)	0 / 591 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 587 (0.00%)	0 / 1 (0.00%)	2 / 591 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia viral			

subjects affected / exposed	1 / 587 (0.17%)	0 / 1 (0.00%)	0 / 591 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus bronchiolitis			
subjects affected / exposed	8 / 587 (1.36%)	0 / 1 (0.00%)	5 / 591 (0.85%)
occurrences causally related to treatment / all	0 / 8	0 / 0	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	3 / 587 (0.51%)	0 / 1 (0.00%)	3 / 591 (0.51%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus bronchitis			
subjects affected / exposed	1 / 587 (0.17%)	0 / 1 (0.00%)	1 / 591 (0.17%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus infection			
subjects affected / exposed	1 / 587 (0.17%)	0 / 1 (0.00%)	0 / 591 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	1 / 587 (0.17%)	0 / 1 (0.00%)	0 / 591 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Salmonellosis			
subjects affected / exposed	1 / 587 (0.17%)	0 / 1 (0.00%)	0 / 591 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillitis			
subjects affected / exposed	1 / 587 (0.17%)	0 / 1 (0.00%)	0 / 591 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			

subjects affected / exposed	1 / 587 (0.17%)	0 / 1 (0.00%)	1 / 591 (0.17%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tracheobronchitis			
subjects affected / exposed	1 / 587 (0.17%)	0 / 1 (0.00%)	0 / 591 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 587 (0.00%)	0 / 1 (0.00%)	3 / 591 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 587 (0.17%)	0 / 1 (0.00%)	2 / 591 (0.34%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			
subjects affected / exposed	3 / 587 (0.51%)	0 / 1 (0.00%)	2 / 591 (0.34%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 587 (0.17%)	0 / 1 (0.00%)	0 / 591 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	V114	V114 + Prevenar 13™	Prevenar 13™
Total subjects affected by non-serious adverse events			
subjects affected / exposed	548 / 587 (93.36%)	1 / 1 (100.00%)	540 / 591 (91.37%)
Nervous system disorders			
Somnolence			
subjects affected / exposed	271 / 587 (46.17%)	0 / 1 (0.00%)	247 / 591 (41.79%)
occurrences (all)	507	0	473

General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	266 / 587 (45.32%)	1 / 1 (100.00%)	264 / 591 (44.67%)
occurrences (all)	455	1	443
Injection site induration			
subjects affected / exposed	246 / 587 (41.91%)	0 / 1 (0.00%)	231 / 591 (39.09%)
occurrences (all)	418	0	392
Injection site pain			
subjects affected / exposed	238 / 587 (40.55%)	0 / 1 (0.00%)	173 / 591 (29.27%)
occurrences (all)	370	0	257
Injection site swelling			
subjects affected / exposed	197 / 587 (33.56%)	0 / 1 (0.00%)	174 / 591 (29.44%)
occurrences (all)	315	0	263
Pyrexia			
subjects affected / exposed	261 / 587 (44.46%)	1 / 1 (100.00%)	251 / 591 (42.47%)
occurrences (all)	447	1	437
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	39 / 587 (6.64%)	0 / 1 (0.00%)	45 / 591 (7.61%)
occurrences (all)	48	0	66
Psychiatric disorders			
Irritability			
subjects affected / exposed	421 / 587 (71.72%)	1 / 1 (100.00%)	392 / 591 (66.33%)
occurrences (all)	1094	1	1038
Infections and infestations			
Rhinitis			
subjects affected / exposed	29 / 587 (4.94%)	0 / 1 (0.00%)	44 / 591 (7.45%)
occurrences (all)	33	0	51
Upper respiratory tract infection			
subjects affected / exposed	9 / 587 (1.53%)	1 / 1 (100.00%)	8 / 591 (1.35%)
occurrences (all)	9	2	8
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	199 / 587 (33.90%)	0 / 1 (0.00%)	198 / 591 (33.50%)
occurrences (all)	354	0	334

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 April 2021	Amendment 2: In response to the COVID-19 global pandemic which impacted the ability of many participants to attend study visits, this amendment expanded the visit windows to allow inclusion of more participants in the immunogenicity analysis.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported