Clinical trial results:
A Phase 3, Multicenter, Randomized, Double-Blind, Active Comparator-Controlled Study to Evaluate the Safety, Tolerability, and Immunogenicity of V114 Followed by Administration of PNEUMOVAX™23 Eight Weeks Later in Adults Infected with HIV (PNEU-WAY)

Summary

EudraCT number	2017-001909-32
Trial protocol	FR
Global end of trial date	17 January 2020

Results information

Result version number	v1 (current)
This version publication date	04 December 2020
First version publication date	04 December 2020

Trial information

Trial identification

Sponsor protocol code	V114-018

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03480802
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Merck Sharp & Dohme Corp.
Sponsor organisation address	2000 Galloping Hill Road, Kenilworth, NJ, United States, 07033
Public contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	17 January 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 September 2019
Global end of trial reached?	Yes
Global end of trial date	17 January 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study is designed to 1) describe the safety, tolerability, and immunogenicity of V114 and Prevnar 13™ in pneumococcal vaccine-naïve adults infected with human immunodeficiency virus (HIV); and to 2) describe the safety, tolerability, and immunogenicity of PNEUMOVAX™23 when administered 8 weeks after receipt of either V114 or Prevnar 13™.

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	06 July 2018
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	France: 39
Country: Number of subjects enrolled	Peru: 68
Country: Number of subjects enrolled	South Africa: 41
Country: Number of subjects enrolled	Thailand: 50
Country: Number of subjects enrolled	United States: 104
Worldwide total number of subjects	302
EEA total number of subjects	39

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)	0
Children (2-11 years)	0

Adolescents (12-17 years)	0
Adults (18-64 years)	291
From 65 to 84 years	11
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Adults 18 years of age or older infected with human immunodeficiency virus (HIV) who did not receive a pneumococcal vaccine prior to study entry were enrolled in this study.

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

Arms

Are arms mutually exclusive?	Yes
Arm title	V114

Arm description:

Participants received a single 0.5 mL intramuscular (IM) injection of V114 on Day 1 (Vaccination 1) and a single 0.5 mL IM injection of PNEUMOVAX™23 at Week 8 (Vaccination 2)

Arm type	Experimental
Investigational medicinal product name	PNEUMOVAX™23
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

23-valent pneumococcal polysaccharide vaccine with serotypes 1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19F, 19A, 20, 22F, 23F, 33F (25 mcg each) in each 0.5 mL dose

Investigational medicinal product name	V114
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

15-valent pneumococcal conjugate vaccine with serotypes 1, 3, 4, 5, 6A, 7F, 9V, 14, 18C, 19F, 19A, 22F, 23F, 33F (2 mcg each), serotype 6B (4 mcg) and Merck Aluminum Phosphate Adjuvant (125 mcg) in each 0.5 mL dose

Arm title	Prevnar 13™

Arm description:

Participants received a single 0.5 mL IM injection of Prevnar 13™ on Day 1 (Vaccination 1) and a single 0.5 mL IM injection of PNEUMOVAX™23 at Week 8 (Vaccination 2)

Arm type	Active comparator
Investigational medicinal product name	Prevnar 13™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

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

Investigational medicinal product name	PNEUMOVAX™23
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

23-valent pneumococcal polysaccharide vaccine with serotypes 1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19F, 19A, 20, 22F, 23F, 33F (25 mcg each) in each 0.5 mL dose

Number of subjects in period 1	V114	Prevnar 13™
Started	152	150
Week 8	150	148
Completed	145	147
Not completed	7	3
Consent withdrawn by subject	2	1
Lost to follow-up	5	1
Relocated	-	1

Baseline characteristics

Reporting groups	
Reporting group title	V114
Reporting group description:	
Participants received a single 0.5 mL intramuscular (IM) injection of V114 on Day 1 (Vaccination 1) and a single 0.5 mL IM injection of PNEUMOVAX™23 at Week 8 (Vaccination 2)	
Reporting group title	Prevnar 13™
Reporting group description:	
Participants received a single 0.5 mL IM injection of Prevnar 13™ on Day 1 (Vaccination 1) and a single 0.5 mL IM injection of PNEUMOVAX™23 at Week 8 (Vaccination 2)	

Reporting group values	V114	Prevnar 13™	Total
Number of subjects	152	150	302
Age Categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	144	147	291
From 65-84 years	8	3	11
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	42.4	41.3	
standard deviation	± 12.5	± 12.3	-
Gender Categorical Units: Subjects			
Female	32	32	64
Male	120	118	238
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	1	1
Asian	24	30	54
Native Hawaiian or Other Pacific Islander	0	2	2
Black or African American	51	43	94
White	41	48	89
More than one race	36	26	62
Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	49	45	94
Not Hispanic or Latino	102	104	206
Unknown or Not Reported	1	1	2

End points

End points reporting groups

Reporting group title	V114
Reporting group description:	
Participants received a single 0.5 mL intramuscular (IM) injection of V114 on Day 1 (Vaccination 1) and a single 0.5 mL IM injection of PNEUMOVAX™23 at Week 8 (Vaccination 2)	
Reporting group title	Prevnar 13™
Reporting group description:	
Participants received a single 0.5 mL IM injection of Prevnar 13™ on Day 1 (Vaccination 1) and a single 0.5 mL IM injection of PNEUMOVAX™23 at Week 8 (Vaccination 2)	

Primary: Percentage of Participants with a Solicited Injection-site Adverse Event After Vaccination 1

End point title	Percentage of Participants with a Solicited Injection-site Adverse Event After Vaccination 1[1]
End point description:	
An adverse event (AE) is any untoward medical occurrence in a patient or clinical study participant, temporally associated with the use of study treatment, whether or not considered related to the study treatment. Solicited injection-site AEs consist of redness/erythema, swelling, and tenderness/pain. The 95% confidence interval (CI) were based on the exact binomial method proposed by Clopper and Pearson. The population analyzed was all randomized participants who received at least 1 dose of the study vaccination they actually received.	
End point type	Primary
End point timeframe:	
Up to 5 days after Vaccination 1	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical analyses were not specified for this primary endpoint because the study was not powered for between group comparisons.

End point values	V114	Prevnar 13™		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	152	150		
Units: Percentage of Participants				
number (confidence interval 95%)				
Injection site erythema	4.6 (1.9 to 9.3)	3.3 (1.1 to 7.6)		
Injection site pain	57.2 (49.0 to 65.2)	51.3 (43.0 to 59.6)		
Injection site swelling	11.8 (7.2 to 18.1)	4.0 (1.5 to 8.5)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants with a Solicited Systemic Adverse Event After Vaccination 1

End point title	Percentage of Participants with a Solicited Systemic Adverse

	Event After Vaccination 1[2]

End point description:

An AE is any untoward medical occurrence in a patient or clinical study participant, temporally associated with the use of study treatment, whether or not considered related to the study treatment. Solicited systemic AEs consist of muscle pain (myalgia), joint pain (arthralgia), headache, and tiredness (fatigue). The 95% CI were based on the exact binomial method proposed by Clopper and Pearson. The population analyzed was all randomized participants who received at least 1 dose of the study vaccination they actually received.

End point type	Primary

End point timeframe:

Up to 14 days after Vaccination 1

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical analyses were not specified for this primary endpoint because the study was not powered for between group comparisons.

End point values	V114	Prevnar 13™		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	152	150		
Units: Percentage of Participants				
number (confidence interval 95%)				
Arthralgia	3.3 (1.1 to 7.5)	4.0 (1.5 to 8.5)		
Fatigue	20.4 (14.3 to 27.7)	13.3 (8.3 to 19.8)		
Headache	13.2 (8.2 to 19.6)	9.3 (5.2 to 15.2)		
Myalgia	12.5 (7.7 to 18.8)	9.3 (5.2 to 15.2)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants with a Vaccine-related Serious Adverse Event After Vaccination 1

End point title	Percentage of Participants with a Vaccine-related Serious Adverse Event After Vaccination 1[3]

End point description:

A serious adverse event (SAE) is an AE that is life-threatening, requires or prolongs an existing hospitalization, results in persistent or significant disability or incapacity, is a congenital anomaly or birth defect, or is another important medical event deemed such by medical or scientific judgment. Relatedness of an SAE to the study vaccine is determined by the investigator. The 95% CI were based on the exact binomial method proposed by Clopper and Pearson. The population analyzed was all randomized participants who received at least 1 dose of the study vaccination they actually received.

End point type	Primary

End point timeframe:

Day 1 up to 8 weeks after Vaccination 1 (Up to 8 weeks)

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical analyses were not specified for this primary endpoint because the study was not powered for between group comparisons.

End point values	V114	Prevnar 13™		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	152	150		
Units: Percentage of Participants				
number (confidence interval 95%)	0 (0.0 to 2.4)	0 (0.0 to 2.4)		

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Titer (GMT) of Serotype-specific Opsonophagocytic Activity (OPA) After Vaccination 1

End point title	Geometric Mean Titer (GMT) of Serotype-specific Opsonophagocytic Activity (OPA) After Vaccination 1[4]

End point description:

Opsonization of pneumococci for phagocytosis is an important mechanism by which antibodies to polysaccharides protect against disease in vivo. Sera from participants was used to measure geometric mean titer (GMT) of 13 serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F) included in V114 and Prevnar 13™; and two serotypes (22F and 33F) which are unique to V114 using the Multiplexed Opsonophagocytic Assay (MOPA). This assay reads the reciprocal of the highest dilution (1/dil) that gives ≥50% bacterial killing, as determined by comparison to assay background controls. The 95% CIs were derived by exponentiating the CIs of the mean of the natural log values based on the t-distribution. The population analyzed was all randomized participants without deviations from the protocol that may substantially affect the results of the immunogenicity endpoint.

End point type	Primary

End point timeframe:

Day 30

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Statistical analyses were not specified for this primary endpoint because the study was not powered for between group comparisons.

End point values	V114	Prevnar 13™		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	152	150		
Units: 1/dil				
geometric mean (confidence interval 95%)				
Serotype 1 (n=131,131)	238.8 (173.1 to 329.3)	200.9 (142.7 to 282.7)		
Serotype 3 (n=131,130)	116.8 (94.9 to 143.7)	72.3 (58.6 to 89.2)		
Serotype 4 (n=130,131)	824.0 (618.8 to 1097.2)	1465.5 (1154.5 to 1860.3)		
Serotype 5 (n=131,130)	336.7 (242.7 to 467.7)	276.7 (197.9 to 386.7)		
Serotype 6A (n=126,128)	6421.0 (4890.4 to 8430.7)	5645.1 (4278.9 to 7447.4)		
Serotype 6B (n=129,130)	4772.9 (3628.3 to 6278.7)	3554.0 (2751.0 to 4591.4)		

Serotype 7F (n=131,131)	6085.8 (4871.6 to 7602.8)	6144.3 (4982.8 to 7576.6)		
Serotype 9V (n=129,128)	2836.3 (2311.5 to 3480.4)	2133.9 (1721.8 to 2644.5)		
Serotype 14 (n=131,130)	3508.7 (2730.6 to 4508.5)	3000.3 (2350.0 to 3830.5)		
Serotype 18C (n=129,129)	3002.2 (2435.5 to 3700.8)	1560.3 (1213.8 to 2005.6)		
Serotype 19A (n=131,131)	4240.7 (3415.4 to 5265.3)	3715.9 (2949.2 to 4681.8)		
Serotype 19F (n=131,131)	2438.6 (1972.7 to 3014.6)	2042.0 (1618.9 to 2575.5)		
Serotype 23F (n=129,127)	1757.4 (1276.1 to 2420.2)	1787.0 (1309.0 to 2437.9)		
Serotype 22F (n=128,116)	3943.7 (3049.2 to 5100.5)	109.3 (66.2 to 180.3)		
Serotype 33F (n=131,129)	11342.4 (9184.3 to 14007.6)	1807.6 (1357.3 to 2407.3)		

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Concentration of Serotype-specific Immunoglobulin G (IgG) After Vaccination 1

End point title	Geometric Mean Concentration of Serotype-specific Immunoglobulin G (IgG) After Vaccination 1[5]

End point description:

The geometric mean concentration of IgG serotype-specific antibodies to the 13 serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F) included in V114 and Prevnar 13™; and two serotypes (22F and 33F) which are unique to V114 were quantitated from participants' sera by multiplex electrochemiluminescence (ECL) using the pneumococcal electrochemiluminescence (PnECL) v2.0 assay, based on the Meso-Scale Discovery technology, which employs disposable multi-spot microtiter plates. The 95% CIs were derived by exponentiating the CIs of the mean of the natural log values based on the t-distribution. The population analyzed was all randomized participants without deviations from the protocol that may substantially affect the results of the immunogenicity endpoint.

End point type	Primary

End point timeframe:

Day 30

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical analyses were not specified for this primary endpoint because the study was not powered for between group comparisons.

End point values	V114	Prevnar 13™		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	152	150		
Units: µg/mL				
geometric mean (confidence interval 95%)				
Serotype 1 (n=139,138)	3.16 (2.48 to 4.01)	4.27 (3.31 to 5.50)		
Serotype 3 (n=139,136)	0.57 (0.48 to 0.68)	0.50 (0.41 to 0.60)		
Serotype 4 (n=138,138)	1.14 (0.90 to 1.44)	2.00 (1.56 to 2.55)		
Serotype 5 (n=139,138)	2.38 (1.89 to 3.01)	2.03 (1.56 to 2.64)		
Serotype 6A (n=139,138)	5.13 (3.73 to 7.04)	4.91 (3.49 to 6.91)		
Serotype 6B (n=139,138)	7.17 (5.34 to 9.63)	5.23 (3.73 to 7.35)		
Serotype 7F (n=139,138)	2.61 (2.00 to 3.41)	3.74 (2.91 to 4.81)		
Serotype 9V (n=139,137)	3.35 (2.71 to 4.14)	3.55 (2.77 to 4.56)		
Serotype 14 (n=139,138)	15.44 (11.69 to 20.39)	15.22 (11.56 to 20.03)		
Serotype 18C (n=139,138)	5.58 (4.33 to 7.18)	5.07 (3.97 to 6.48)		
Serotype 19A (n=139,138)	9.09 (7.08 to 11.67)	9.61 (7.36 to 12.56)		
Serotype 19F (n=139,138)	6.41 (4.89 to 8.39)	6.21 (4.73 to 8.15)		
Serotype 23F (n=139,138)	3.92 (2.94 to 5.22)	4.90 (3.54 to 6.77)		
Serotype 22F (n=139,137)	3.97 (3.06 to 5.15)	0.20 (0.17 to 0.25)		
Serotype 33F (n=139,138)	6.83 (5.14 to 9.07)	0.77 (0.62 to 0.95)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with a Solicited Injection-site Adverse Event After Vaccination 2

End point title	Percentage of Participants with a Solicited Injection-site Adverse Event After Vaccination 2

End point description:

An AE is any untoward medical occurrence in a patient or clinical study participant, temporally associated with the use of study treatment, whether or not considered related to the study treatment. Solicited injection-site AEs consist of redness/erythema, swelling, and tenderness/pain. The 95% confidence interval (CI) were based on the exact binomial method proposed by Clopper and Pearson. The population analyzed was all randomized participants who received at least 1 dose of the study vaccination they actually received.

End point type	Secondary

End point timeframe:

Up to 5 days after Vaccination 2 (Up to Day 61)

End point values	V114	Prevnar 13™		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	150	148		
Units: Percentage of Participants				
number (confidence interval 95%)				
Injection site erythema	10.0 (5.7 to 16.0)	12.2 (7.4 to 18.5)		
Injection site pain	53.3 (45.0 to 61.5)	61.5 (53.1 to 69.4)		
Injection site swelling	20.0 (13.9 to 27.3)	29.1 (21.9 to 37.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with a Solicited Systemic Adverse Event After Vaccination 2

End point title	Percentage of Participants with a Solicited Systemic Adverse Event After Vaccination 2

End point description:

An AE is any untoward medical occurrence in a patient or clinical study participant, temporally associated with the use of study treatment, whether or not considered related to the study treatment. Solicited systemic AEs consist of muscle pain (myalgia), joint pain (arthralgia), headache, and tiredness (fatigue). The 95% CI were based on the exact binomial method proposed by Clopper and Pearson. The population analyzed was all randomized participants who received at least 1 dose of the study vaccination they actually received.

End point type	Secondary

End point timeframe:

Up to 14 days after Vaccination 2 (Up to Day 70)

End point values	V114	Prevnar 13™		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	150	148		
Units: Percentage of Participants				
number (confidence interval 95%)				
Arthralgia	2.7 (0.7 to 6.7)	1.4 (0.2 to 4.8)		
Fatigue	12.7 (7.8 to 19.1)	10.8 (6.3 to 17.0)		
Headache	8.7 (4.7 to 14.4)	8.8 (4.8 to 14.6)		
Myalgia	11.3 (6.7 to 17.5)	12.2 (7.4 to 18.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with a Vaccine-related Serious Adverse Event After Vaccination 2

End point title	Percentage of Participants with a Vaccine-related Serious Adverse Event After Vaccination 2

End point description:

A serious adverse event (SAE) is an AE that is life-threatening, requires or prolongs an existing hospitalization, results in persistent or significant disability or incapacity, is a congenital anomaly or birth defect, or is another important medical event deemed such by medical or scientific judgment. Relatedness of an SAE to the study vaccine is determined by the investigator. The 95% CI were based on the exact binomial method proposed by Clopper and Pearson. The population analyzed was all randomized participants who received at least 1 dose of the study vaccination they actually received.

End point type	Secondary

End point timeframe:

Week 8 up to Month 6

End point values	V114	Prevnar 13™		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	150	148		
Units: Percentage of Participants				
number (confidence interval 95%)	0 (0.0 to 2.4)	0 (0.0 to 2.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titer of Serotype-specific OPA After Vaccination 2

End point title	Geometric Mean Titer of Serotype-specific OPA After Vaccination 2

End point description:

Opsonization of pneumococci for phagocytosis is an important mechanism by which antibodies to polysaccharides protect against disease in vivo. Sera from participants was used to measure GMT of 13 serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F) included in V114 and Prevnar 13™; and two serotypes (22F and 33F) which are unique to V114 using the MOPA. The MOPA reads the reciprocal of the highest dilution that gives ≥50% bacterial killing, as determined by comparison to assay background controls. The population analyzed was all randomized participants without deviations from the protocol that may substantially affect the results of the outcome measure.

End point type	Secondary

End point timeframe:

Week 12

End point values	V114	Prevnar 13™		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	150	148		
Units: 1/dil				
geometric mean (confidence interval 95%)				
Serotype 1 (n=122,117)	212.0 (160.5 to 280.2)	154.0 (111.6 to 212.4)		
Serotype 3 (n=123,117)	102.8 (83.0 to 127.2)	96.6 (79.5 to 117.4)		
Serotype 4 (n=122,117)	915.4 (722.9 to 1159.1)	984.7 (772.1 to 1255.7)		
Serotype 5 (n=123,117)	418.1 (312.1 to 560.3)	274.5 (199.9 to 376.8)		
Serotype 6A (n=118,113)	4065.4 (3052.1 to 5415.1)	4593.2 (3543.0 to 5954.7)		
Serotype 6B (n=122,117)	3661.1 (2735.1 to 4900.6)	2826.4 (2202.7 to 3626.8)		
Serotype 7F (n=122,117)	5983.5 (4788.9 to 7476.1)	5516.5 (4522.2 to 6729.5)		
Serotype 9V (n=120,117)	2454.8 (2008.7 to 3000.0)	1929.9 (1567.7 to 2375.7)		
Serotype 14 (n=123,117)	3634.0 (2935.6 to 4498.5)	2539.3 (1960.6 to 3288.9)		
Serotype 18C (n=122,115)	2511.5 (1958.7 to 3220.3)	1753.8 (1428.6 to 2153.1)		
Serotype 19A (n=123,117)	3358.1 (2679.6 to 4208.4)	3300.3 (2638.7 to 4127.7)		
Serotype 19F (n=123,116)	2230.7 (1803.6 to 2759.0)	1994.1 (1630.7 to 2438.4)		
Serotype 23F (n=120,116)	1641.2 (1217.2 to 2212.9)	1266.5 (944.3 to 1698.5)		
Serotype 22F (n=121,116)	3399.9 (2697.6 to 4285.0)	2952.7 (2207.7 to 3949.1)		
Serotype 33F (n=123,117)	10576.3 (8383.1 to 13343.4)	11926.3 (9085.9 to 15654.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Concentration of Serotype-specific IgG After

Vaccination 2

End point title	Geometric Mean Concentration of Serotype-specific IgG After Vaccination 2

End point description:

The geometric mean concentration of IgG serotype-specific antibodies to the 13 serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F) included in V114 and Prevnar 13™; and two serotypes (22F and 33F) which are unique to V114 were quantitated from participants' sera by multiplex ECL using the PnECL v2.0 assay, based on the Meso-Scale Discovery technology, which employs disposable multi-spot microtiter plates. The population analyzed was all randomized participants without deviations from the protocol that may substantially affect the results of the immunogenicity endpoint.

End point type	Secondary

End point timeframe:

Week 12

End point values	V114	Prevnar 13™		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	150	148		
Units: µg/mL				
geometric mean (confidence interval 95%)				
Serotype 1 (n=130,129)	2.80 (2.25 to 3.49)	4.04 (3.27 to 5.00)		
Serotype 3 (n=130,128)	0.51 (0.43 to 0.61)	0.59 (0.50 to 0.70)		
Serotype 4 (n=130,129)	1.26 (1.10 to 1.57)	1.61 (1.31 to 1.98)		
Serotype 5 (n=130,129)	2.61 (2.08 to 3.28)	2.13 (1.69 to 2.68)		
Serotype 6A (n=130,129)	3.12 (2.27 to 4.30)	3.71 (2.74 to 5.03)		
Serotype 6B (n=130,129)	4.69 (3.52 to 6.25)	4.35 (3.23 to 5.86)		
Serotype 7F (n=130,129)	2.45 (1.91 to 3.15)	3.17 (2.60 to 3.87)		
Serotype 9V (n=130,128)	2.92 (2.39 to 3.57)	3.24 (2.62 to 4.01)		
Serotype 14 (n=130,129)	13.68 (10.34 to 18.10)	14.37 (11.25 to 18.36)		
Serotype 18C (n=130,129)	3.96 (3.08 to 5.09)	3.96 (3.18 to 4.95)		
Serotype 19A (n=130,129)	7.23 (5.80 to 9.02)	8.54 (6.80 to 10.72)		
Serotype 19F (n=130,129)	5.19 (4.06 to 6.62)	5.84 (4.67 to 7.30)		
Serotype 23F (n=130,129)	3.21 (2.42 to 4.25)	3.74 (2.85 to 4.91)		
Serotype 22F (n=130,129)	3.94 (3.07 to 5.05)	3.50 (2.75 to 4.45)		
Serotype 33F (n=130,129)	6.18 (4.72 to 8.09)	9.20 (7.19 to 11.77)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

V114 and Prevnar 13™: NSAEs Day 1 up to 14 days after vaccination 1; SAEs Day 1 up to Week 8. V114 (Post-PPV23) and Prevnar 13™ (Post-PPV23): NSAEs week 8 up to 14 days after vaccination 2; SAEs Week 8 vaccination up to Month 6. Mortality: Up to Month 6.

Adverse event reporting additional description:

The population reported was all randomized participants who received study intervention at the specified timepoint. Adverse events were reported (1) following administration of either V114 or Prevnar 13™ and (2) following administration of PNEUMOVAX™23 (PPV23).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.1

Reporting groups

Reporting group title	V114

Reporting group description:

Participants received a single 0.5 mL intramuscular (IM) injection of V114 on Day 1 (Vaccination 1).

Reporting group title	Prevnar 13™

Reporting group description:

Participants received a single 0.5 mL IM injection of Prevnar 13™ on Day 1 (Vaccination 1).

Reporting group title	V114 (Post-PPV23)

Reporting group description:

Participants received a single 0.5 mL IM injection of V114 on Day 1 (Vaccination 1) and a single 0.5 mL IM injection of PNEUMOVAX™23 (PPV23) at Week 8 (Vaccination 2).

Reporting group title	Prevnar 13™ (Post-PPV23)

Reporting group description:

Participants received a single 0.5 mL IM injection of Prevnar 13™ on Day 1 (Vaccination 1) and a single 0.5 mL IM injection of PPV23 at Week 8 (Vaccination 2).

Serious adverse events	V114	Prevnar 13™	V114 (Post-PPV23)
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 152 (1.97%)	0 / 150 (0.00%)	2 / 150 (1.33%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Foot fracture			
subjects affected / exposed	0 / 152 (0.00%)	0 / 150 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Dry gangrene			

subjects affected / exposed	0 / 152 (0.00%)	0 / 150 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Transient ischaemic attack			
subjects affected / exposed	1 / 152 (0.66%)	0 / 150 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 152 (0.00%)	0 / 150 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 152 (0.00%)	0 / 150 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Suicide attempt			
subjects affected / exposed	1 / 152 (0.66%)	0 / 150 (0.00%)	0 / 150 (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			
Chondrocalcinosis pyrophosphate			
subjects affected / exposed	1 / 152 (0.66%)	0 / 150 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 152 (0.00%)	0 / 150 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster			

subjects affected / exposed	0 / 152 (0.00%)	0 / 150 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis			
subjects affected / exposed	0 / 152 (0.00%)	0 / 150 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Soft tissue infection			
subjects affected / exposed	0 / 152 (0.00%)	0 / 150 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Prevnar 13™ (Post-PPV23)		
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 148 (4.05%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Foot fracture			
subjects affected / exposed	1 / 148 (0.68%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Dry gangrene			
subjects affected / exposed	1 / 148 (0.68%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Transient ischaemic attack			
subjects affected / exposed	0 / 148 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Chest pain			

subjects affected / exposed	1 / 148 (0.68%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 148 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Suicide attempt			
subjects affected / exposed	0 / 148 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Chondrocalcinosis pyrophosphate			
subjects affected / exposed	0 / 148 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 148 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Herpes zoster			
subjects affected / exposed	2 / 148 (1.35%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Peritonitis			
subjects affected / exposed	1 / 148 (0.68%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Soft tissue infection			

subjects affected / exposed	1 / 148 (0.68%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	V114	Prevnar 13™	V114 (Post-PPV23)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	103 / 152 (67.76%)	88 / 150 (58.67%)	88 / 150 (58.67%)
Nervous system disorders			
Headache			
subjects affected / exposed	20 / 152 (13.16%)	14 / 150 (9.33%)	13 / 150 (8.67%)
occurrences (all)	23	15	14
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	31 / 152 (20.39%)	20 / 150 (13.33%)	19 / 150 (12.67%)
occurrences (all)	34	23	20
Injection site erythema			
subjects affected / exposed	8 / 152 (5.26%)	5 / 150 (3.33%)	15 / 150 (10.00%)
occurrences (all)	8	5	15
Injection site pain			
subjects affected / exposed	88 / 152 (57.89%)	78 / 150 (52.00%)	80 / 150 (53.33%)
occurrences (all)	100	86	97
Injection site swelling			
subjects affected / exposed	18 / 152 (11.84%)	6 / 150 (4.00%)	30 / 150 (20.00%)
occurrences (all)	18	6	30
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	19 / 152 (12.50%)	14 / 150 (9.33%)	17 / 150 (11.33%)
occurrences (all)	21	15	18

Non-serious adverse events	Prevnar 13™ (Post-PPV23)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	99 / 148 (66.89%)		
Nervous system disorders			

Headache			
subjects affected / exposed	13 / 148 (8.78%)		
occurrences (all)	13		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	16 / 148 (10.81%)		
occurrences (all)	16		
Injection site erythema			
subjects affected / exposed	18 / 148 (12.16%)		
occurrences (all)	18		
Injection site pain			
subjects affected / exposed	92 / 148 (62.16%)		
occurrences (all)	101		
Injection site swelling			
subjects affected / exposed	43 / 148 (29.05%)		
occurrences (all)	43		
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	18 / 148 (12.16%)		
occurrences (all)	18		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 July 2018	Amendment 1: Removed the collection of medical device incidents from the protocol; made clarifications and editorial revisions.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported