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 Children Infected with Human Immunodeficiency Virus (HIV) (PNEU-WAY PED)

Summary

EudraCT number	2019-000341-12
Trial protocol	Outside EU/EEA
Global end of trial date	03 May 2021

Results information

Result version number	v1 (current)
This version publication date	28 October 2021
First version publication date	28 October 2021

Trial information

Trial identification

Sponsor protocol code	V114-030

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03921424
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)	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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	03 May 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 May 2021
Global end of trial reached?	Yes
Global end of trial date	03 May 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This is a study of V114 in children infected with HIV. Participants were randomly assigned in a 1:1 ratio to receive either V114 or Prevnar 13™ followed 8 weeks later by a single dose of PNEUMOVAX™23. The primary objectives of this study were to evaluate the safety and tolerability of V114 in children 6 to 17 years of age inclusive infected with HIV and to evaluate the anti-pneumococcal polysaccharide (PnPs) serotype-specific Immunoglobulin G (IgG) Geometric Mean Concentrations (GMCs) at 30 days following vaccination with V114 or Prevnar 13™ by each vaccination group. There were no formal hypotheses.

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	05 November 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	Thailand: 127
Country: Number of subjects enrolled	South Africa: 191
Country: Number of subjects enrolled	Ukraine: 89
Worldwide total number of subjects	407
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	122
Adolescents (12-17 years)	285

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

Subject disposition

Recruitment

Recruitment details:

This study recruited 6-17 year old participants with HIV.

Pre-assignment

Screening details:

407 participants were randomized in a 1:1 ratio to receive either V114 or Prevnar 13™ on Day 1 and PNEUMOVAX™23 at Week 8.

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

Blinding implementation details:

Study was double-blinded with in-house blinding procedures.

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	23-valent pneumococcal polysaccharide vaccine (PPV23)
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

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

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

Dosage and administration details:

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

Arm title	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	13-valent pneumococcal conjugate vaccine (PCV13)
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:	
13-valent pneumococcal conjugate vaccine containing 13 serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F) in each 0.5 mL dose	
Investigational medicinal product name	PNEUMOVAX™23
Investigational medicinal product code	
Other name	PPV23
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
23-valent pneumococcal polysaccharide vaccine containing 23 serotypes (1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19A, 19F, 20, 22F, 23F, 33F) in each 0.5 mL dose	

Number of subjects in period 1	V114	Prevnar 13™
Started	203	204
Vaccination 1 - (Day 1)	203	204
Vaccination 2 - (Week 8)	203	202
Completed	203	201
Not completed	0	3
Withdrawal By Parent/Guardian	-	2
Lost to follow-up	-	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	203	204	407
Age Categorical Units: Participants			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	60	62	122
Adolescents (12-17 years)	143	142	285
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	12.7	12.6	
standard deviation	± 2.7	± 3.0	-
Gender Categorical Units: Participants			
Male	107	105	212
Female	96	99	195
Race Units: Subjects			
Asian	62	66	128
Black Or African American	88	78	166
Multiple	12	9	21
White	40	49	89
Missing	1	2	3
Ethnicity Units: Subjects			
Hispanic Or Latino	0	1	1
Not Hispanic Or Latino	201	203	404
Not Reported	2	0	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 Following Vaccination With V114 or Prevnar 13™

End point title	Percentage of Participants with a Solicited Injection-Site Adverse Event Following Vaccination With V114 or Prevnar 13™[1]
End point description:	
An adverse event (AE) is any untoward medical occurrence in a participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention. Following Vaccination 1 with either V114 or Prevnar 13™, the percentage of participants with solicited injection-site AEs was assessed. The solicited injection-site AEs assessed were redness/erythema, hard lump/induration, tenderness/pain, and swelling. All randomized participants who received at least 1 dose of study vaccination were analyzed.	
End point type	Primary
End point timeframe:	
Through 14 Days after Vaccination 1 (Up to Day 14)	

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: No between-group comparisons were performed for this end point.

End point values	V114	Prevnar 13™		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	203	204		
Units: Percentage of Participants				
number (confidence interval 95%)				
Injection site redness/erythema	9.4 (5.7 to 14.2)	5.9 (3.1 to 10.0)		
Injection site hard lump/induration	10.3 (6.5 to 15.4)	6.4 (3.4 to 10.7)		
Injection site tenderness/pain	55.2 (48.1 to 62.1)	53.9 (46.8 to 60.9)		
Injection site swelling	28.6 (22.5 to 35.3)	21.6 (16.1 to 27.9)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants with a Solicited Systemic Adverse Event Following Vaccination With V114 or Prevnar 13™

End point title	Percentage of Participants with a Solicited Systemic Adverse Event Following Vaccination With V114 or Prevnar 13™[2]

End point description:

An AE is any untoward medical occurrence in a participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention. Following Vaccination 1 with either V114 or Prevnar 13™, the percentage of participants with solicited systemic AEs was assessed. The solicited systemic AEs assessed were joint pain/arthralgia, tiredness/fatigue, headache, muscle pain/myalgia, and hives or welts/urticaria. All randomized participants who received at least 1 dose of study vaccination were analyzed.

End point type	Primary

End point timeframe:

Through 14 Days after Vaccination 1 (Up to Day 14)

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: No between-group comparisons were performed for this end point.

End point values	V114	Prevnar 13™		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	203	204		
Units: Percentage of Participants				
number (confidence interval 95%)				
Joint pain/arthralgia	9.4 (5.7 to 14.2)	10.3 (6.5 to 15.3)		
Tiredness/fatigue	7.9 (4.6 to 12.5)	8.3 (4.9 to 13.0)		
Headache	14.8 (10.2 to 20.4)	10.8 (6.9 to 15.9)		
Muscle pain/myalgia	34.0 (27.5 to 41.0)	25.5 (19.7 to 32.0)		
Hives or welts/urticaria	0.5 (0.0 to 2.7)	1.5 (0.3 to 4.2)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants with a Vaccine-related Serious Adverse Event (SAE) Following Vaccination 1 (V114 or Prevnar 13™) or Vaccination 2 (PNEUMOVAX™23) Through Completion of Study

End point title	Percentage of Participants with a Vaccine-related Serious Adverse Event (SAE) Following Vaccination 1 (V114 or Prevnar 13™) or Vaccination 2 (PNEUMOVAX™23) Through Completion of Study[3]

End point description:

An SAE is an AE that results in death, is life-threatening, requires or prolongs an existing hospitalization, results in persistent or significant disability or incapacity, is a congenital anomaly or birth defect, or is another important medical event deemed such by medical or scientific judgment. The percentage of participants with a vaccine-related SAE following Vaccination 1 (with either V114 or Prevnar 13™) or Vaccination 2 (PNEUMOVAX™23) through completion of study participation was reported. All randomized participants who received at least 1 dose of the relevant study vaccination for the timepoint of interest were analyzed. Two participants in the Prevnar 13™ group did not receive PNEUMOVAX™23 and therefore were not analyzed for Vaccination 2.

End point type	Primary

End point timeframe:

Through 6 Months after Vaccination 1 (Up to Day 194)

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: No between-group comparisons were performed for this end point.

End point values	V114	Prevnar 13™		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	203	204		
Units: Percentage of Participants				
number (confidence interval 95%)				
Vaccination 1 (n = 203, 204)	0.0 (0.0 to 1.8)	0.0 (0.0 to 1.8)		
Vaccination 2 (n = 203, 202)	0.0 (0.0 to 1.8)	0.0 (0.0 to 1.8)		

Statistical analyses

No statistical analyses for this end point

Primary: Anti-PnPs Serotype-specific IgG Geometric Mean Concentrations (GMCs) at 30 Days Following Vaccination With V114 or Prevnar 13™

End point title	Anti-PnPs Serotype-specific IgG Geometric Mean Concentrations (GMCs) at 30 Days Following Vaccination With V114 or Prevnar 13™[4]

End point description:

The GMC of serotype-specific IgG for the serotypes contained in V114 (13 serotypes shared with Prevnar 13™ and 2 serotypes unique to V114) was determined using an electrochemiluminescence assay. All randomized participants without protocol deviations that could have substantially impacted the results of the immunogenicity endpoint and who had sufficient data to perform the analyses were analyzed.

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: No between-group comparisons were performed for this end point.

End point values	V114	Prevnar 13™		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	203	204		
Units: µg/mL				
geometric mean (confidence interval 95%)				
Serotype 1 (Shared) (n=194, 196)	2.17 (1.89 to 2.48)	3.26 (2.82 to 3.77)		
Serotype 3 (Shared) (n=194, 196)	1.05 (0.93 to 1.19)	0.84 (0.73 to 0.97)		
Serotype 4 (Shared) (n=194, 196)	2.59 (2.23 to 3.00)	4.27 (3.57 to 5.11)		
Serotype 5 (Shared) (n=194, 196)	2.94 (2.44 to 3.54)	2.78 (2.30 to 3.37)		
Serotype 6A (Shared) (n=194, 196)	7.98 (6.30 to 10.11)	7.56 (6.06 to 9.45)		

Serotype 6B (Shared) (n=194, 196)	11.44 (9.07 to 14.43)	6.92 (5.45 to 8.79)		
Serotype 7F (Shared) (n=194, 196)	4.84 (4.10 to 5.71)	5.00 (4.29 to 5.83)		
Serotype 9V (Shared) (n=194, 196)	4.15 (3.56 to 4.85)	4.78 (4.03 to 5.66)		
Serotype 14 (Shared) (n=194, 196)	20.38 (16.39 to 25.35)	18.29 (14.43 to 23.17)		
Serotype 18C (Shared) (n=194, 196)	5.18 (4.32 to 6.20)	5.15 (4.29 to 6.18)		
Serotype 19A (Shared) (n=194, 196)	14.20 (11.81 to 17.07)	14.78 (12.45 to 17.54)		
Serotype 19F (Shared) (n=194, 196)	9.76 (8.03 to 11.85)	8.61 (7.28 to 10.18)		
Serotype 23F (Shared) (n=194, 196)	6.71 (5.42 to 8.31)	6.35 (5.14 to 7.85)		
Serotype 22F (Unique to V114) (n=194, 193)	9.28 (7.76 to 11.09)	0.24 (0.20 to 0.29)		
Serotype 33F (Unique to V114) (n=194, 196)	4.53 (3.80 to 5.39)	0.29 (0.25 to 0.33)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with a Solicited Injection-Site Adverse Event Following Vaccination With PNEUMOVAX™23

End point title	Percentage of Participants with a Solicited Injection-Site Adverse Event Following Vaccination With PNEUMOVAX™23

End point description:

An AE is any untoward medical occurrence in a participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention. Following Vaccination 2 with PNEUMOVAX™23 (PPV23), the percentage of participants with solicited injection-site AEs was assessed. The solicited injection-site AEs assessed were redness/erythema, hard lump/induration, tenderness/pain, and swelling. All randomized participants who received at least 1 dose of the relevant study vaccination for the timepoint of interest were analyzed. Two participants in the Prevnar 13™ group did not receive PNEUMOVAX™23 and therefore were not included in the analysis for this end point.

End point type	Secondary

End point timeframe:

Through 14 Days after Vaccination 2 (Up to Day 84)

End point values	V114	Prevnar 13™		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	203	202		
Units: Percentage of Participants				
number (confidence interval 95%)				
Injection site redness/erythema	10.3 (6.5 to 15.4)	12.4 (8.2 to 17.7)		
Injection site hard lump/induration	18.2 (13.2 to 24.2)	13.4 (9.0 to 18.8)		
Injection site tenderness/pain	51.7 (44.6 to 58.8)	55.0 (47.8 to 61.9)		

Injection site swelling	47.3 (40.3 to 54.4)	34.7 (28.1 to 41.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with a Solicited Systemic Adverse Event Following Vaccination With PNEUMOVAX™23

End point title	Percentage of Participants with a Solicited Systemic Adverse Event Following Vaccination With PNEUMOVAX™23

End point description:

An AE is any untoward medical occurrence in a participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention. Following Vaccination 2 with PNEUMOVAX™23, the percentage of participants with solicited systemic AEs was assessed. The solicited systemic AEs assessed were joint pain/arthralgia, tiredness/fatigue, headache, muscle pain/myalgia, and hives or welts/urticaria. All randomized participants who received at least 1 dose of the relevant study vaccination for the timepoint of interest were analyzed. Two participants in the Prevnar 13™ group did not receive PNEUMOVAX™23 and therefore were not included in the analysis for this end point.

End point type	Secondary

End point timeframe:

Through 14 Days after Vaccination 2 (Up to Day 84)

End point values	V114	Prevnar 13™		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	203	202		
Units: Percentage of Participants				
number (confidence interval 95%)				
Joint pain/arthralgia	12.8 (8.5 to 18.2)	8.4 (5.0 to 13.1)		
Tiredness/fatigue	12.3 (8.1 to 17.6)	11.4 (7.4 to 16.6)		
Headache	10.3 (6.5 to 15.4)	9.4 (5.8 to 14.3)		
Muscle pain/myalgia	43.3 (36.4 to 50.5)	39.1 (32.3 to 46.2)		
Hives or welts/urticaria	0.0 (0.0 to 1.8)	0.5 (0.0 to 2.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-PnPs Serotype-specific Opsonophagocytic Activity (OPA) Geometric Mean Titers (GMTs) at 30 Days Following Vaccination With V114 or Prevnar 13™

End point title	Anti-PnPs Serotype-specific Opsonophagocytic Activity (OPA) Geometric Mean Titers (GMTs) at 30 Days Following Vaccination With V114 or Prevnar 13™

End point description:

The GMT of serotype-specific OPA for the serotypes contained in V114 (13 serotypes shared with Prevnar 13™ and 2 serotypes unique to V114) was determined using a multiplexed opsonophagocytic assay. All randomized participants without protocol deviations that could have substantially impacted the results of the immunogenicity endpoint and who had sufficient data to perform the analyses were analyzed.

End point type	Secondary

End point timeframe:

Day 30

End point values	V114	Prevnar 13™		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	203	204		
Units: Titers (1/dil)				
geometric mean (confidence interval 95%)				
Serotype 1 (Shared) (n=164, 160)	353.4 (278.4 to 448.7)	398.3 (313.5 to 506.1)		
Serotype 3 (Shared) (n=163, 158)	330.0 (284.4 to 383.0)	301.5 (255.5 to 355.7)		
Serotype 4 (Shared) (n=164, 159)	6078.3 (5106.1 to 7235.4)	9172.8 (7582.8 to 11096.1)		
Serotype 5 (Shared) (n=164, 160)	847.6 (671.1 to 1070.4)	642.1 (490.9 to 839.9)		
Serotype 6A (Shared) (n=163, 159)	14274.6 (12014.1 to 16960.4)	11915.4 (10160.9 to 13973.0)		
Serotype 6B (Shared) (n=164, 160)	17636.5 (14728.7 to 21118.3)	15052.9 (12719.6 to 17814.2)		
Serotype 7F (Shared) (n=164, 160)	17574.4 (15234.2 to 20274.0)	18519.3 (16010.9 to 21420.8)		
Serotype 9V (Shared) (n=164, 160)	4800.0 (4201.0 to 5484.4)	5879.7 (4853.9 to 7122.2)		
Serotype 14 (Shared) (n=164, 160)	18444.3 (15257.3 to 22297.0)	17920.8 (14874.4 to 21591.2)		
Serotype 18C (Shared) (n=163, 160)	4556.2 (3794.1 to 5471.5)	3543.0 (2919.6 to 4299.5)		
Serotype 19A (Shared) (n=164, 160)	8176.4 (6778.3 to 9862.8)	8690.2 (7382.3 to 10229.8)		
Serotype 19F (Shared) (n=164, 159)	3711.8 (3178.0 to 4335.2)	3277.6 (2833.1 to 3791.8)		
Serotype 23F (Shared) (n=162, 160)	11693.1 (9483.8 to 14417.1)	11933.8 (9597.5 to 14838.8)		
Serotype 22F (Unique to V114) (n=164, 142)	10791.3 (9157.2 to 12716.9)	503.1 (330.1 to 766.8)		
Serotype 33F (Unique to V114) (n=162, 159)	36357.0 (31146.2 to 42439.6)	5520.6 (4659.5 to 6540.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-PnPs Serotype-specific OPA GMTs at 30 Days Following Vaccination With PNEUMOVAX™23

End point title	Anti-PnPs Serotype-specific OPA GMTs at 30 Days Following Vaccination With PNEUMOVAX™23

End point description:

The GMT of serotype-specific OPA for the serotypes contained in V114 (13 serotypes shared with Prevnar 13™ and 2 serotypes unique to V114) was determined using a multiplexed opsonophagocytic assay. All randomized participants without protocol deviations that could have substantially impacted the results of the immunogenicity endpoint and who had sufficient data to perform the analyses were analyzed. Two participants in the Prevnar 13™ group did not receive PNEUMOVAX™23 and therefore were not included in the analysis for this end point.

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	203	202		
Units: Titers (1/dil)				
geometric mean (confidence interval 95%)				
Serotype 1 (Shared) (n=164, 162)	326.4 (267.0 to 399.0)	337.0 (272.3 to 417.1)		
Serotype 3 (Shared) (n=164, 161)	327.2 (278.9 to 383.9)	384.8 (333.0 to 444.6)		
Serotype 4 (Shared) (n=164, 162)	5445.7 (4663.7 to 6358.8)	7526.8 (6309.7 to 8978.7)		
Serotype 5 (Shared) (n=165, 162)	985.6 (813.6 to 1193.8)	939.5 (737.3 to 1197.3)		
Serotype 6A (Shared) (n=164, 162)	10208.7 (8703.8 to 11973.7)	10699.8 (9010.5 to 12705.7)		
Serotype 6B (Shared) (n=164, 162)	13774.8 (11661.6 to 16271.0)	12745.8 (10887.3 to 14921.6)		
Serotype 7F (Shared) (n=165, 162)	17415.9 (15091.4 to 20098.5)	19140.5 (16778.5 to 21835.0)		
Serotype 9V (Shared) (n=165, 161)	5135.9 (4328.2 to 6094.3)	6152.2 (5219.6 to 7251.4)		
Serotype 14 (Shared) (n=165, 161)	17207.5 (14074.5 to 21037.9)	16461.2 (13695.1 to 19785.9)		

Serotype 18C (Shared) (n=165, 161)	3635.1 (3103.0 to 4258.5)	3369.0 (2844.0 to 3990.9)		
Serotype 19A (Shared) (n=164, 162)	7613.7 (6414.6 to 9036.9)	8838.0 (7592.6 to 10287.6)		
Serotype 19F (Shared) (n=165, 162)	3694.8 (3212.9 to 4248.9)	3904.4 (3382.3 to 4507.1)		
Serotype 23F (Shared) (n=163, 161)	10216.7 (8465.7 to 12329.8)	10086.0 (8334.0 to 12206.2)		
Serotype 22F (Unique to V114) (n=165, 162)	8756.1 (7419.0 to 10334.1)	6958.0 (5941.5 to 8148.5)		
Serotype 33F (Unique to V114) (n=163, 162)	34173.6 (29554.9 to 39514.0)	30651.0 (26240.5 to 35802.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-PnPs Serotype-specific IgG GMCs at 30 Days Following Vaccination With PNEUMOVAX™23

End point title	Anti-PnPs Serotype-specific IgG GMCs at 30 Days Following Vaccination With PNEUMOVAX™23

End point description:

The GMC of serotype-specific IgG for the serotypes contained in V114 (13 serotypes shared with Prevnar 13™ and 2 serotypes unique to V114) was determined using an electrochemiluminescence assay. All randomized participants without protocol deviations that could have substantially impacted the results of the immunogenicity endpoint and who had sufficient data to perform the analyses were analyzed. Two participants in the Prevnar 13™ group did not receive PNEUMOVAX™23 and therefore were not included in the analysis for this end point.

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	203	202		
Units: µg/mL				
geometric mean (confidence interval 95%)				
Serotype 1 (Shared) (n=192, 183)	2.58 (2.31 to 2.88)	3.33 (2.95 to 3.75)		
Serotype 3 (Shared) (n=192, 183)	1.10 (0.97 to 1.24)	1.08 (0.94 to 1.24)		
Serotype 4 (Shared) (n=192, 182)	2.36 (2.08 to 2.69)	3.61 (3.09 to 4.23)		
Serotype 5 (Shared) (n=192, 183)	3.01 (2.58 to 3.52)	3.24 (2.75 to 3.82)		

Serotype 6A (Shared) (n=192, 183)	4.67 (3.74 to 5.84)	4.91 (3.94 to 6.11)		
Serotype 6B (Shared) (n=192, 183)	7.12 (5.75 to 8.81)	4.96 (3.96 to 6.22)		
Serotype 7F (Shared) (n=192, 183)	4.10 (3.55 to 4.72)	4.27 (3.71 to 4.92)		
Serotype 9V (Shared) (n=192, 183)	3.69 (3.20 to 4.25)	4.52 (3.89 to 5.24)		
Serotype 14 (Shared) (n=192, 183)	18.88 (15.43 to 23.09)	19.89 (16.00 to 24.72)		
Serotype 18C (Shared) (n=192, 183)	3.75 (3.18 to 4.43)	4.11 (3.48 to 4.85)		
Serotype 19A (Shared) (n=192, 183)	11.23 (9.48 to 13.31)	12.19 (10.38 to 14.32)		
Serotype 19F (Shared) (n=192, 183)	8.56 (7.26 to 10.08)	7.98 (6.83 to 9.33)		
Serotype 23F (Shared) (n=192, 183)	4.40 (3.63 to 5.34)	4.83 (3.96 to 5.88)		
Serotype 22F (Unique to V114) (n=192, 183)	8.18 (7.10 to 9.42)	10.32 (8.67 to 12.29)		
Serotype 33F (Unique to V114) (n=192, 183)	3.76 (3.23 to 4.38)	6.18 (5.23 to 7.30)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Non-serious adverse events: Up to 14 days after each vaccination; Serious adverse events and deaths (all-causes): Through 6 months after Vaccination 1 (Up to Day 194).

Adverse event reporting additional description:

The analysis population for deaths (all-causes) included all randomized participants. The analysis population for AEs included all randomized participants who received at least 1 dose of study vaccination. All randomized participants received treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

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 title	V114 (Post-PNEUMOVAX™23)

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™ (Post-PNEUMOVAX™23)

Reporting group description:

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

Serious adverse events	V114	Prevnar 13™	V114 (Post-PNEUMOVAX™23)
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 203 (0.49%)	1 / 204 (0.49%)	2 / 203 (0.99%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Hodgkin's disease			
subjects affected / exposed	0 / 203 (0.00%)	0 / 204 (0.00%)	1 / 203 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Serous retinal detachment			

subjects affected / exposed	0 / 203 (0.00%)	1 / 204 (0.49%)	0 / 203 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Gastrointestinal inflammation			
subjects affected / exposed	0 / 203 (0.00%)	0 / 204 (0.00%)	1 / 203 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Abnormal uterine bleeding			
subjects affected / exposed	1 / 203 (0.49%)	0 / 204 (0.00%)	0 / 203 (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			
Suicidal ideation			
subjects affected / exposed	0 / 203 (0.00%)	0 / 204 (0.00%)	0 / 203 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Diarrhoea infectious			
subjects affected / exposed	0 / 203 (0.00%)	0 / 204 (0.00%)	0 / 203 (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-PNEUMOVAX™23)		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 202 (0.99%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Hodgkin's disease			
subjects affected / exposed	0 / 202 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eye disorders			

Serous retinal detachment			
subjects affected / exposed	0 / 202 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Gastrointestinal inflammation			
subjects affected / exposed	0 / 202 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Abnormal uterine bleeding			
subjects affected / exposed	0 / 202 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Suicidal ideation			
subjects affected / exposed	1 / 202 (0.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Diarrhoea infectious			
subjects affected / exposed	1 / 202 (0.50%)		
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-PNEUMOVAX™23)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	158 / 203 (77.83%)	138 / 204 (67.65%)	152 / 203 (74.88%)
Nervous system disorders			
Headache			
subjects affected / exposed	30 / 203 (14.78%)	22 / 204 (10.78%)	21 / 203 (10.34%)
occurrences (all)	34	28	25
General disorders and administration site conditions			

Fatigue			
subjects affected / exposed	16 / 203 (7.88%)	17 / 204 (8.33%)	25 / 203 (12.32%)
occurrences (all)	16	19	30
Injection site erythema			
subjects affected / exposed	19 / 203 (9.36%)	12 / 204 (5.88%)	21 / 203 (10.34%)
occurrences (all)	20	13	21
Injection site induration			
subjects affected / exposed	21 / 203 (10.34%)	13 / 204 (6.37%)	37 / 203 (18.23%)
occurrences (all)	22	13	37
Injection site pain			
subjects affected / exposed	112 / 203 (55.17%)	110 / 204 (53.92%)	105 / 203 (51.72%)
occurrences (all)	122	117	110
Injection site swelling			
subjects affected / exposed	58 / 203 (28.57%)	44 / 204 (21.57%)	96 / 203 (47.29%)
occurrences (all)	59	49	97
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	19 / 203 (9.36%)	21 / 204 (10.29%)	26 / 203 (12.81%)
occurrences (all)	20	24	26
Myalgia			
subjects affected / exposed	69 / 203 (33.99%)	52 / 204 (25.49%)	88 / 203 (43.35%)
occurrences (all)	72	56	91

Non-serious adverse events	Prevnar 13™ (Post-PNEUMOVAX™23)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	154 / 202 (76.24%)		
Nervous system disorders			
Headache			
subjects affected / exposed	19 / 202 (9.41%)		
occurrences (all)	22		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	23 / 202 (11.39%)		
occurrences (all)	23		
Injection site erythema			

subjects affected / exposed	25 / 202 (12.38%)		
occurrences (all)	25		
Injection site induration			
subjects affected / exposed	27 / 202 (13.37%)		
occurrences (all)	27		
Injection site pain			
subjects affected / exposed	111 / 202 (54.95%)		
occurrences (all)	117		
Injection site swelling			
subjects affected / exposed	70 / 202 (34.65%)		
occurrences (all)	70		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	17 / 202 (8.42%)		
occurrences (all)	17		
Myalgia			
subjects affected / exposed	79 / 202 (39.11%)		
occurrences (all)	80		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported