Clinical trial results:
A Phase 3 Clinical Study to Evaluate the Safety, Tolerability, and Immunogenicity of V116 in Pneumococcal Vaccine-Experienced Adults 50 Years of Age or Older

Summary

EudraCT number	2021-006679-41
Trial protocol	IT ES FR
Global end of trial date	16 May 2023

Results information

Result version number	v1 (current)
This version publication date	19 May 2024
First version publication date	19 May 2024

Trial information

Trial identification

Sponsor protocol code	V116-006

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05420961
WHO universal trial number (UTN)	-

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	16 May 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 May 2023
Global end of trial reached?	Yes
Global end of trial date	16 May 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This a study of V116 in adults ≥50 years of age who previously received a pneumococcal vaccination ≥1 year before enrollment. The primary objectives of this study are to evaluate the safety, tolerability, and immunogenicity of V116.

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	12 July 2022
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	Canada: 75
Country: Number of subjects enrolled	Spain: 51
Country: Number of subjects enrolled	France: 4
Country: Number of subjects enrolled	Israel: 99
Country: Number of subjects enrolled	Italy: 33
Country: Number of subjects enrolled	Japan: 63
Country: Number of subjects enrolled	Korea, Republic of: 100
Country: Number of subjects enrolled	Taiwan: 67
Country: Number of subjects enrolled	United States: 225
Worldwide total number of subjects	717
EEA total number of subjects	88

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)	210
From 65 to 84 years	495
85 years and over	12

Subject disposition

Recruitment

Recruitment details:

717 adults were randomized to 1 of 3 cohorts. The All Participants as Treated (APaT) population consists of all randomized participants who received at least 1 dose of study vaccination.

Pre-assignment

Screening details:

1 participant randomized to PCV15 in Cohort 1 incorrectly received V116; per protocol participant was included in Cohort 1 V116. 1 participant randomized to PCV15 in Cohort 1 received PPSV23 (intervention for Cohort 2); per protocol participant was excluded from APaT population, since intervention received was not 1 of the 2 designated in Cohort 1.

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:

Cohorts 1 and 2 were double-blind. Cohort 3 was unblinded, open-label.

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1: V116

Arm description:

Participants received a single 0.5 mL intramuscular (IM) injection of V116 on Day 1. Participants in this arm received PPSV23 (pneumococcal vaccine, polyvalent [23-valent], PNEUMOVAX™23) prior to the enrollment.

Arm type	Experimental
Investigational medicinal product name	V116
Investigational medicinal product code	
Other name	Pneumococcal 21-valent Conjugate Vaccine
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Pneumococcal 21-valent conjugate vaccine with 4 µg of each of the pneumococcal polysaccharides (PnPs) antigen: 3, 6A, 7F, 8, 9N, 10A, 11A, 12F, 15A, 15C, 16F, 17F, 19A, 20A, 22F, 23A, 23B, 24F, 31, 33F, and 35B in each 0.5 mL sterile solution

Arm title	Cohort 1: PCV15

Arm description:

Participants received a single 0.5 mL IM injection of PCV15 (pneumococcal 15-valent conjugate vaccine; VAXNEUVANCE™) on Day 1. Participants in this arm received PPSV23 prior to the enrollment.

Arm type	Active comparator
Investigational medicinal product name	PCV15
Investigational medicinal product code	
Other name	VAXNEUVANCE™
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Pneumococcal 15-valent conjugate vaccine with 2 µg of each of the PnPs antigen: 1, 3, 4, 5, 6A, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F, 33F, and 4 µg of 6B in each 0.5 mL sterile suspension

Arm title	Cohort 2: V116

Arm description:	
Participants received a single 0.5 mL IM injection of V116 on Day 1. Participants in this arm received PCV13 (pneumococcal 13-valent conjugate vaccine; PREVNAR 13™) prior to the enrollment.	
Arm type	Experimental
Investigational medicinal product name	V116
Investigational medicinal product code	
Other name	Pneumococcal 21-valent Conjugate Vaccine
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
Pneumococcal 21-valent conjugate vaccine with 4 µg of each of the pneumococcal polysaccharides (PnPs) antigen: 3, 6A, 7F, 8, 9N, 10A, 11A, 12F, 15A, 15C, 16F, 17F, 19A, 20A, 22F, 23A, 23B, 24F, 31, 33F, and 35B in each 0.5 mL sterile solution	
Arm title	Cohort 2: PPSV23
Arm description:	
Participants received a single 0.5 mL IM injection of PPSV23 on Day 1. Participants in this arm received PCV13 prior to the enrollment.	
Arm type	Active comparator
Investigational medicinal product name	PPSV23
Investigational medicinal product code	
Other name	PNEUMOVAX™23
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
Pneumococcal 23-valent vaccine with 25 µg of each of the PnPs antigen: 1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19A, 19F, 20, 22F, 23F, and 33F in each 0.5 mL sterile solution	
Arm title	Cohort 3: V116
Arm description:	
Participants received a single 0.5 mL IM injection of V116 on Day 1. Participants in this arm received PCV15, PCV13+PPSV23, PCV15+PPSV23, or PPSV23+PCV13 prior to the enrollment.	
Arm type	Experimental
Investigational medicinal product name	V116
Investigational medicinal product code	
Other name	Pneumococcal 21-valent Conjugate Vaccine
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
Pneumococcal 21-valent conjugate vaccine with 4 µg of each of the pneumococcal polysaccharides (PnPs) antigen: 3, 6A, 7F, 8, 9N, 10A, 11A, 12F, 15A, 15C, 16F, 17F, 19A, 20A, 22F, 23A, 23B, 24F, 31, 33F, and 35B in each 0.5 mL sterile solution	

Number of subjects in period 1	Cohort 1: V116	Cohort 1: PCV15	Cohort 2: V116
Started	231	119	176
Day 1 - Vaccinated with V116	229	1 [1]	174
Day 1 - Vaccinated with PCV15	0 [2]	117 [3]	0 [4]
Day 1 - Vaccinated with PPSV23	0 [5]	1 [6]	0 [7]
Completed	229	118	173
Not completed	2	1	3

Consent withdrawn by subject	2	1	1
Randomized by mistake without study treatment	-	-	1
Lost to follow-up	-	-	1

Number of subjects in period 1	Cohort 2: PPSV23	Cohort 3: V116
Started	85	106
Day 1 - Vaccinated with V116	0 [8]	105
Day 1 - Vaccinated with PCV15	0 [9]	0 [10]
Day 1 - Vaccinated with PPSV23	85	0 [11]
Completed	85	105
Not completed	0	1
Consent withdrawn by subject	-	-
Randomized by mistake without study treatment	-	1
Lost to follow-up	-	-

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: Cohort 1: V116 group participants could have been considered to complete the study without receipt of PCV15 on Day 1.

[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: This participant inadvertently received PPSV23 on Day 1. Cohort 1: PCV15 group participants could have been considered to complete the study without receipt of PPSV23 on Day 1.

[3] - 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: Cohort 2: V116 group participants could have been considered to complete the study without receipt of PCV15 on Day 1.

[4] - 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: Cohort 2: V116 group participants could have been considered to complete the study without receipt of PPSV23 on Day 1.

[5] - 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: Cohort 3: V116 group participants could have been considered to complete the study without receipt of PCV15 on Day 1.

[6] - 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: Cohort 3: V116 group participants could have been considered to complete the study without receipt of PPSV23 on Day 1.

[7] - 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: Cohort 1: V116 group participants could have been considered to complete the study without receipt of PPSV23 on Day 1.

[8] - 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: This participant inadvertently received V116 on Day 1. Cohort 1: PCV15 group participants could have been considered to complete the study without receipt of V116 on Day 1.

[9] - 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: Cohort 2: PPSV23 group participants could have been considered to complete the study without receipt of V116 on Day 1.

[10] - 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: Cohort 2: PPSV23 group participants could have been considered to complete the study without receipt of PCV15 on Day 1.

[11] - 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: Two participants randomized to receive PCV115, inadvertently received incorrect vaccine on Day 1. Cohort 1: PCV15 group participants could have been considered to complete the study without receipt of V116 and PPSV23 on Day 1.

Baseline characteristics

Reporting groups	
Reporting group title	Cohort 1: V116
Reporting group description:	
Participants received a single 0.5 mL intramuscular (IM) injection of V116 on Day 1. Participants in this arm received PPSV23 (pneumococcal vaccine, polyvalent [23-valent], PNEUMOVAX™23) prior to the enrollment.	
Reporting group title	Cohort 1: PCV15
Reporting group description:	
Participants received a single 0.5 mL IM injection of PCV15 (pneumococcal 15-valent conjugate vaccine; VAXNEUVANCE™) on Day 1. Participants in this arm received PPSV23 prior to the enrollment.	
Reporting group title	Cohort 2: V116
Reporting group description:	
Participants received a single 0.5 mL IM injection of V116 on Day 1. Participants in this arm received PCV13 (pneumococcal 13-valent conjugate vaccine; PREVNAR 13™) prior to the enrollment.	
Reporting group title	Cohort 2: PPSV23
Reporting group description:	
Participants received a single 0.5 mL IM injection of PPSV23 on Day 1. Participants in this arm received PCV13 prior to the enrollment.	
Reporting group title	Cohort 3: V116
Reporting group description:	
Participants received a single 0.5 mL IM injection of V116 on Day 1. Participants in this arm received PCV15, PCV13+PPSV23, PCV15+PPSV23, or PPSV23+PCV13 prior to the enrollment.	

Reporting group values	Cohort 1: V116	Cohort 1: PCV15	Cohort 2: V116
Number of subjects	231	119	176
Age categorical Units: Subjects			
Adults (18-64 years)	48	25	81
From 65-84 years	179	91	95
85 years and over	4	3	0
Age Continuous Units: Years			
arithmetic mean	68.8	69.0	65.4
standard deviation	± 7.5	± 7.1	± 7.8
Sex: Female, Male Units: Participants			
Female	117	60	101
Male	114	59	75
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	96	47	55
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	6	3	3
White	127	69	118
More than one race	2	0	0
Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB)			

Units: Subjects			
Hispanic or Latino	22	17	34
Not Hispanic or Latino	207	102	142
Unknown or Not Reported	2	0	0

Reporting group values	Cohort 2: PPSV23	Cohort 3: V116	Total
Number of subjects	85	106	717
Age categorical Units: Subjects			
Adults (18-64 years)	39	17	210
From 65-84 years	46	84	495
85 years and over	0	5	12
Age Continuous Units: Years			
arithmetic mean	65.4	71.0	
standard deviation	± 6.6	± 7.6	-
Sex: Female, Male Units: Participants			
Female	49	56	383
Male	36	50	334
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	25	13	236
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	1	6	19
White	59	86	459
More than one race	0	1	3
Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	16	14	103
Not Hispanic or Latino	69	92	612
Unknown or Not Reported	0	0	2

End points

End points reporting groups

Reporting group title	Cohort 1: V116
Reporting group description:	
Participants received a single 0.5 mL intramuscular (IM) injection of V116 on Day 1. Participants in this arm received PPSV23 (pneumococcal vaccine, polyvalent [23-valent], PNEUMOVAX™23) prior to the enrollment.	
Reporting group title	Cohort 1: PCV15
Reporting group description:	
Participants received a single 0.5 mL IM injection of PCV15 (pneumococcal 15-valent conjugate vaccine; VAXNEUVANCE™) on Day 1. Participants in this arm received PPSV23 prior to the enrollment.	
Reporting group title	Cohort 2: V116
Reporting group description:	
Participants received a single 0.5 mL IM injection of V116 on Day 1. Participants in this arm received PCV13 (pneumococcal 13-valent conjugate vaccine; PREVNAR 13™) prior to the enrollment.	
Reporting group title	Cohort 2: PPSV23
Reporting group description:	
Participants received a single 0.5 mL IM injection of PPSV23 on Day 1. Participants in this arm received PCV13 prior to the enrollment.	
Reporting group title	Cohort 3: V116
Reporting group description:	
Participants received a single 0.5 mL IM injection of V116 on Day 1. Participants in this arm received PCV15, PCV13+PPSV23, PCV15+PPSV23, or PPSV23+PCV13 prior to the enrollment.	

Primary: Percentage of Participants with Solicited Injection-site Adverse Events (AEs)

End point title	Percentage of Participants with Solicited Injection-site Adverse Events (AEs)[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 intervention, whether or not considered related to the study intervention. Following any injection with either V116, PCV15, or PPSV23 the percentage of participants with solicited injection-site AEs was assessed. The solicited injection-site AEs assessed were erythema, pain, and swelling. All randomized participants who received at least 1 dose of study vaccination were analyzed.	
End point type	Primary
End point timeframe:	
Up to 5 days post-vaccination	

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 statistical analyses were performed for this endpoint.

End point values	Cohort 1: V116	Cohort 1: PCV15	Cohort 2: V116	Cohort 2: PPSV23
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	230	117	174	85
Units: Percentage of Participants				
number (not applicable)				
Injection site erythema	7.4	7.7	7.5	9.4
Injection site pain	35.7	43.6	41.4	47.1
Injection site swelling	8.3	8.5	4.6	16.5

End point values	Cohort 3: V116			
Subject group type	Reporting group			
Number of subjects analysed	105			
Units: Percentage of Participants				
number (not applicable)				
Injection site erythema	7.6			
Injection site pain	43.8			
Injection site swelling	10.5			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants with Solicited Systemic AEs

End point title	Percentage of Participants with Solicited Systemic AEs[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 intervention, whether or not considered related to the study intervention. Following any of the injections with either V116, PCV15, or PPSV23, the percentage of participants with solicited systemic AEs was assessed. The solicited systemic AEs assessed were fatigue, headache, myalgia, and pyrexia. All randomized participants who received at least 1 dose of study vaccination were analyzed.

End point type	Primary

End point timeframe:

Up to 5 days post-vaccination

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 statistical analyses were performed for this endpoint.

End point values	Cohort 1: V116	Cohort 1: PCV15	Cohort 2: V116	Cohort 2: PPSV23
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	230	117	174	85
Units: Percentage of Participants				
number (not applicable)				
Fatigue	14.3	17.1	19.0	12.9
Headache	7.0	9.4	10.3	11.8
Myalgia	7.4	2.6	9.8	9.4
Pyrexia	1.7	2.6	2.9	1.2

End point values	Cohort 3: V116			
Subject group type	Reporting group			
Number of subjects analysed	105			

Units: Percentage of Participants				
number (not applicable)				
Fatigue	21.9			
Headache	8.6			
Myalgia	8.6			
Pyrexia	0.0			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants with Vaccine-related Serious Adverse Events (SAEs)

End point title	Percentage of Participants with Vaccine-related Serious Adverse Events (SAEs)[3]

End point description:

A serious adverse event (SAE) is any untoward medical occurrence that, at any dose, results in death, is life threatening, requires inpatient hospitalization or prolongs existing hospitalization, results in persistent or significant disability/incapacity, is a congenital anomaly/birth defect, or is another important medical event. The percentage of participants with one or more SAE that were assessed by the investigator to be at least possibly related to the study vaccination are presented. All randomized participants who received at least 1 dose of study vaccination were analyzed.

End point type	Primary

End point timeframe:

Up to ~180 days

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 statistical analyses were performed for this endpoint.

End point values	Cohort 1: V116	Cohort 1: PCV15	Cohort 2: V116	Cohort 2: PPSV23
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	230	117	174	85
Units: Percentage of Participants				
number (not applicable)	0.4	0.0	0.0	0.0

End point values	Cohort 3: V116			
Subject group type	Reporting group			
Number of subjects analysed	105			
Units: Percentage of Participants				
number (not applicable)	0.0			

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

OPA for the serotypes contained in V116 were determined using a multiplex opsonophagocytic assay (MOPA). GMT is defined as geometric mean titer (1/dil). Serotype-specific OPA GMTs with 95% confidence intervals are presented. 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:

30 Days post-vaccination

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 statistical analyses were performed for this endpoint.

End point values	Cohort 1: V116	Cohort 1: PCV15	Cohort 2: V116	Cohort 2: PPSV23
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	215	115	166	78
Units: Titers				
geometric mean (confidence interval 95%)				
Serotype 3 (n=197, 103, 149, 75, 85)	262.1 (224.0 to 306.8)	226.3 (182.0 to 281.4)	391.1 (332.8 to 459.6)	583.1 (453.5 to 749.6)
Serotype 6A (n=191, 94, 152, 74, 93)	1653.5 (1347.2 to 2029.4)	2076.1 (1571.4 to 2742.8)	3624.0 (3099.2 to 4237.7)	1812.3 (1226.6 to 2677.6)
Serotype 7F (n=209, 110, 150, 70, 96)	2184.4 (1891.4 to 2522.8)	1750.3 (1404.7 to 2181.0)	3129.8 (2609.9 to 3753.3)	4057.0 (3211.2 to 5125.6)
Serotype 19A (n=204, 109, 158, 74, 93)	1513.8 (1318.4 to 1738.1)	2022.9 (1634.1 to 2504.3)	2528.9 (2201.7 to 2904.9)	3241.5 (2646.0 to 3971.0)
Serotype 22F (n=206, 108, 143, 71, 99)	1983.8 (1698.3 to 2317.4)	1595.6 (1227.1 to 2074.6)	4389.2 (3541.1 to 5440.3)	2524.0 (1834.5 to 3472.5)
Serotype 33F (n=188, 99, 131, 59, 88)	4311.9 (3625.1 to 5128.9)	3397.2 (2665.3 to 4330.0)	8162.9 (6407.2 to 10399.7)	8761.9 (6157.4 to 12468.1)
Serotype 8 (n=208, 113, 161, 75, 98)	1273.0 (1115.1 to 1453.3)	345.8 (250.5 to 477.5)	2320.1 (1987.3 to 2708.7)	2723.2 (2197.4 to 3374.8)
Serotype 9N (n=191, 111, 143, 58, 90)	3805.1 (3324.0 to 4356.0)	2176.5 (1809.6 to 2617.9)	7214.4 (6062.9 to 8584.6)	6482.5 (4908.9 to 8560.7)
Serotype 10A n=209, 112, 155, 73, 96)	1986.2 (1637.7 to 2408.9)	467.5 (337.0 to 648.5)	3976.8 (3360.7 to 4705.8)	1797.6 (1136.2 to 2843.9)
Serotype 11A (n=197, 100, 142, 71, 87)	1998.5 (1696.9 to 2353.8)	335.6 (228.9 to 491.8)	2846.6 (2411.0 to 3360.8)	1736.6 (1367.1 to 2206.1)
Serotype 12F (n=212, 114, 160, 73, 99)	981.8 (782.4 to 1232.1)	80.5 (54.0 to 120.1)	2252.6 (2120.5 to 3072.9)	1402.5 (912.2 to 2156.4)
Serotype 15A (n=175, 93, 134, 63, 86)	4184.9 (3548.3 to 4935.6)	877.2 (616.2 to 1248.7)	6185.2 (5179.3 to 7386.6)	1668.2 (1234.4 to 2254.5)

Serotype 15C (n= 206, 110, 152, 72, 89)	2307.8 (1878.4 to 2835.4)	539.6 (371.1 to 784.6)	4334.4 (3563.8 to 5271.5)	1470.4 (978.6 to 2209.3)
Serotype 16F (n=187, 107, 146, 74, 89)	3060.5 (2633.8 to 3556.3)	392.3 (301.3 to 510.8)	4626.5 (3861.8 to 5542.6)	832.8 (604.3 to 1147.6)
Serotype 17F (n=194, 108, 125, 67, 82)	3599.8 (3134.5 to 4134.3)	939.6 (693.7 to 1272.6)	5963.8 (5036.6 to 7061.7)	4367.3 (3372.5 to 5655.7)
Serotype 20A (n=195, 110, 138, 72, 88)	2847.4 (2433.3 to 3331.8)	1058.9 (829.9 to 1351.1)	6005.5 (4919.8 to 7330.8)	3393.9 (2536.9 to 4540.5)
Serotype 23A (n=202, 91, 156, 60, 86)	2363.9 (1857.4 to 3008.5)	310.2 (202.1 to 476.0)	4253.4 (3417.6 to 5293.5)	433.6 (247.5 to 759.5)
Serotype 23B (n=197, 110, 160, 75, 97)	673.2 (517.1 to 876.4)	153.0 (98.7 to 237.1)	1530.7 (1196.5 to 1958.3)	203.9 (127.6 to 325.6)
Serotype 24F (n=201, 97, 151, 63, 90)	1822.6 (1411.6 to 2353.3)	106.6 (69.7 to 162.9)	2746.1 (2257.9 to 3339.9)	48.5 (28.6 to 82.1)
Serotype 31 (n=194, 108, 146, 68, 90)	3018.4 (2473.6 to 3683.3)	113.2 (74.5 to 172.1)	4413.5 (3530.2 to 5517.7)	171.8 (99.9 to 295.6)
Serotype 35B (n=194, 107, 148, 76, 90)	6703.1 (5732.7 to 7837.8)	1019.1 (739.9 to 1403.7)	8143.5 (6761.4 to 9808.1)	1527.7 (1169.5 to 1995.5)

End point values	Cohort 3: V116			
Subject group type	Reporting group			
Number of subjects analysed	99			
Units: Titers				
geometric mean (confidence interval 95%)				
Serotype 3 (n=197, 103, 149, 75, 85)	318.3 (250.0 to 405.3)			
Serotype 6A (n=191, 94, 152, 74, 93)	2097.3 (1693.4 to 2597.6)			
Serotype 7F (n=209, 110, 150, 70, 96)	2051.3 (1630.2 to 2581.0)			
Serotype 19A (n=204, 109, 158, 74, 93)	1533.8 (1272.4 to 1848.9)			
Serotype 22F (n=206, 108, 143, 71, 99)	1913.5 (1453.5 to 2519.0)			
Serotype 33F (n=188, 99, 131, 59, 88)	4654.3 (3532.1 to 6133.1)			
Serotype 8 (n=208, 113, 161, 75, 98)	1486.8 (1230.5 to 1796.6)			
Serotype 9N (n=191, 111, 143, 58, 90)	4054.5 (3389.4 to 4850.2)			
Serotype 10A n=209, 112, 155, 73, 96)	2564.0 (1959.1 to 3355.6)			

Serotype 11A (n=197, 100, 142, 71, 87)	2373.0 (1905.4 to 2955.4)			
Serotype 12F (n=212, 114, 160, 73, 99)	1235.3 (948.3 to 1609.2)			
Serotype 15A (n=175, 93, 134, 63, 86)	4328.6 (3378.7 to 5545.7)			
Serotype 15C (n= 206, 110, 152, 72, 89)	2191.9 (1573.2 to 3053.9)			
Serotype 16F (n=187, 107, 146, 74, 89)	2477.0 (1887.2 to 3251.2)			
Serotype 17F (n=194, 108, 125, 67, 82)	3836.7 (3063.4 to 4805.1)			
Serotype 20A (n=195, 110, 138, 72, 88)	2433.4 (1880.5 to 3148.9)			
Serotype 23A (n=202, 91, 156, 60, 86)	3967.2 (2764.8 to 5692.7)			
Serotype 23B (n=197, 110, 160, 75, 97)	844.0 (608.2 to 1171.4)			
Serotype 24F (n=201, 97, 151, 63, 90)	2041.5 (1500.8 to 2777.1)			
Serotype 31 (n=194, 108, 146, 68, 90)	3285.5 (2485.0 to 4343.8)			
Serotype 35B (n=194, 107, 148, 76, 90)	5836.8 (4693.6 to 7258.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Concentration (GMC) of Serotype-specific Immunoglobulin G (IgG)

End point title	Geometric Mean Concentration (GMC) of Serotype-specific Immunoglobulin G (IgG)

End point description:

The geometric mean concentration (GMC) of serotype-specific immunoglobulin G (IgG) for the serotypes contained in V116 was determined using a pneumococcal electrochemiluminescence (PnECL) assay. Serotype-specific pneumococcal IgG GMCs with 95% confidence intervals are presented. 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:

30 Days post-vaccination

End point values	Cohort 1: V116	Cohort 1: PCV15	Cohort 2: V116	Cohort 2: PPSV23
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	220	117	167	81
Units: µg/mL				
geometric mean (confidence interval 95%)				
Serotype 3 (n=220, 117, 167, 81, 99)	0.87 (0.77 to 0.99)	0.80 (0.65 to 0.97)	0.89 (0.77 to 1.03)	1.58 (1.25 to 2.00)
Serotype 6A (219, 117, 167, 81, 99)	4.69 (3.72 to 5.90)	7.69 (5.60 to 10.57)	7.81 (6.30 to 9.68)	5.24 (3.62 to 7.56)
Serotype 7F (219, 117, 167, 81, 99)	5.71 (4.89 to 6.68)	6.45 (5.08 to 8.19)	5.65 (4.75 to 6.73)	8.34 (6.57 to 10.59)
Serotype 19A (219, 117, 167, 81, 99)	8.54 (7.33 to 9.95)	11.97 (9.40 to 15.24)	9.12 (7.70 to 10.81)	12.41 (9.57 to 16.11)
Serotype 22F (n=219, 117, 167, 81, 99)	4.41 (3.69 to 5.28)	4.33 (3.37 to 5.56)	5.38 (4.34 to 6.66)	2.87 (2.12 to 3.87)
Serotype 33F (n=220, 117, 167, 81, 99)	13.36 (11.22 to 15.91)	12.72 (10.37 to 15.61)	15.04 (12.31 to 18.37)	13.92 (10.23 to 18.94)
Serotype 8 (n=220, 117, 167, 81, 99)	9.58 (8.21 to 11.17)	3.56 (2.74 to 4.62)	11.29 (9.28 to 13.73)	14.47 (10.86 to 19.27)
Serotype 9N (n=217, 117, 167, 81, 99)	7.06 (5.92 to 8.43)	3.59 (2.83 to 4.55)	8.48 (6.89 to 10.44)	7.32 (5.47 to 9.78)
Serotype 10A (n=220, 117, 167, 81, 99)	9.86 (7.99 to 12.18)	2.77 (2.12 to 3.63)	18.21 (14.30 to 23.18)	7.29 (4.94 to 10.74)
Serotype 11A (n=219, 117, 167, 81, 99)	7.16 (6.09 to 8.42)	2.06 (1.65 to 2.58)	9.13 (7.44 to 11.22)	3.95 (2.98 to 5.23)
Serotype 12F (n=220, 117, 167, 81, 99)	1.46 (1.18 to 1.81)	0.41 (0.30 to 0.55)	1.91 (1.44 to 2.53)	1.01 (0.65 to 1.56)
Serotype 15A (n=220, 117, 167, 81, 99)	16.35 (13.45 to 19.88)	1.56 (1.19 to 2.05)	20.24 (15.92 to 25.75)	2.15 (1.52 to 3.03)
Serotype 15C (n=219, 117, 166, 81, 99)	11.08 (9.01 to 13.62)	3.25 (2.37 to 4.45)	16.67 (12.78 to 21.76)	4.31 (2.91 to 6.38)
Serotype 16F (n=218, 117, 166, 81, 99)	4.69 (3.75 to 5.87)	0.37 (0.28 to 0.48)	4.04 (3.19 to 5.10)	0.30 (0.22 to 0.41)
Serotype 17F (n=219, 117, 167, 81, 99)	13.20 (11.18 to 15.58)	2.68 (2.08 to 3.46)	14.96 (12.37 to 18.08)	7.23 (5.26 to 9.92)
Serotype 20A (n=219, 117, 167, 81, 99)	14.83 (12.37 to 17.77)	4.93 (3.83 to 6.36)	22.21 (17.77 to 27.75)	10.73 (7.48 to 15.41)
Serotype 23A (n=219, 117, 166, 81, 99)	5.38 (4.19 to 6.90)	0.75 (0.55 to 1.02)	6.03 (4.55 to 7.99)	0.62 (0.43 to 0.90)
Serotype 23B (n=219, 117, 167, 81, 99)	6.66 (5.53 to 8.03)	2.61 (1.96 to 3.48)	6.00 (4.91 to 7.33)	2.31 (1.75 to 3.06)
Serotype 24F (n=219, 117, 167, 81, 99)	10.05 (7.59 to 13.32)	0.49 (0.39 to 0.61)	7.48 (5.45 to 10.46)	0.31 (0.23 to 0.42)
Serotype 31 (n=217, 117, 167, 81, 99)	4.48 (3.66 to 5.48)	0.37 (0.30 to 0.47)	3.58 (2.87 to 4.46)	0.32 (0.24 to 0.44)
Serotype 35B (n=218, 117, 167, 81, 99)	26.31 (21.60 to 32.04)	1.45 (1.18 to 1.78)	24.55 (20.09 to 30.01)	1.45 (1.17 to 1.80)

End point values	Cohort 3: V116			
Subject group type	Reporting group			
Number of subjects analysed	99			
Units: µg/mL				
geometric mean (confidence interval 95%)				

Serotype 3 (n=220, 117, 167, 81, 99)	0.85 (0.70 to 1.03)			
Serotype 6A (219, 117, 167, 81, 99)	5.48 (4.27 to 7.03)			
Serotype 7F (219, 117, 167, 81, 99)	5.07 (4.12 to 6.23)			
Serotype 19A (219, 117, 167, 81, 99)	8.06 (6.50 to 9.98)			
Serotype 22F (n=219, 117, 167, 81, 99)	3.08 (2.36 to 4.01)			
Serotype 33F (n=220, 117, 167, 81, 99)	9.66 (7.53 to 12.40)			
Serotype 8 (n=220, 117, 167, 81, 99)	7.48 (5.87 to 9.53)			
Serotype 9N (n=217, 117, 167, 81, 99)	4.15 (3.23 to 5.34)			
Serotype 10A (n=220, 117, 167, 81, 99)	10.03 (7.21 to 13.98)			
Serotype 11A (n=219, 117, 167, 81, 99)	4.78 (3.79 to 6.03)			
Serotype 12F (n=220, 117, 167, 81, 99)	0.96 (0.70 to 1.31)			
Serotype 15A (n=220, 117, 167, 81, 99)	11.16 (7.91 to 15.75)			
Serotype 15C (n=219, 117, 166, 81, 99)	6.51 (4.72 to 8.99)			
Serotype 16F (n=218, 117, 166, 81, 99)	2.46 (1.78 to 3.41)			
Serotype 17F (n=219, 117, 167, 81, 99)	9.92 (7.86 to 12.53)			
Serotype 20A (n=219, 117, 167, 81, 99)	12.16 (8.99 to 16.46)			
Serotype 23A (n=219, 117, 166, 81, 99)	4.25 (2.88 to 6.26)			
Serotype 23B (n=219, 117, 167, 81, 99)	5.05 (3.90 to 6.54)			
Serotype 24F (n=219, 117, 167, 81, 99)	6.12 (3.84 to 9.75)			
Serotype 31 (n=217, 117, 167, 81, 99)	3.66 (2.64 to 5.08)			
Serotype 35B (n=218, 117, 167, 81, 99)	18.15 (13.61 to 24.21)			

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Fold Rise in Serotype-specific Opsonophagocytic Activity (OPA)

End point title	Geometric Mean Fold Rise in Serotype-specific Opsonophagocytic Activity (OPA)

End point description:

Activity for the serotypes contained in V116 was determined using a multiplex opsonophagocytic assay (MOPA). Geometric mean fold rise (GMFR) is defined as the geometric mean of the ratio of concentration at Day 30 after vaccination divided by concentration at baseline. The GMFRs in OPA responses from baseline to 30 days post-vaccination with 95% confidence intervals are presented. 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 1 (Baseline) and 30 days post-vaccination

End point values	Cohort 1: V116	Cohort 1: PCV15	Cohort 2: V116	Cohort 2: PPSV23
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	212	115	164	76
Units: Ratio				
geometric mean (confidence interval 95%)				
Serotype 3 (n=164, 91, 131, 68, 76)	4.4 (3.7 to 5.3)	4.0 (3.1 to 5.3)	6.2 (5.0 to 7.6)	7.5 (5.3 to 10.5)
Serotype 6A (n=171, 87, 136, 66, 89)	6.2 (5.0 to 7.7)	7.1 (4.9 to 10.3)	4.2 (3.3 to 5.3)	1.8 (1.4 to 2.4)
Serotype 7F (n=200, 102, 146, 69, 92)	4.1 (3.3 to 5.1)	3.9 (2.8 to 5.4)	4.6 (3.6 to 5.9)	4.2 (3.1 to 5.8)
Serotype 19A (n=194, 104, 149, 72, 90)	2.4 (2.0 to 2.8)	3.3 (2.5 to 4.4)	2.8 (2.3 to 3.3)	3.6 (2.7 to 4.7)
Serotype 22F (n=193, 102, 124, 64, 94)	7.0 (5.5 to 9.0)	7.1 (4.8 to 10.6)	26.3 (17.7 to 39.2)	14.8 (8.7 to 25.1)
Serotype 33F (n=177, 93, 125, 50, 85)	2.2 (1.8 to 2.6)	1.7 (1.3 to 2.4)	6.3 (4.8 to 8.4)	9.2 (5.6 to 15.3)
Serotype 8 (n=198, 108, 151, 71, 96)	2.8 (2.4 to 3.4)	0.9 (0.7 to 1.0)	16.6 (12.2 to 22.7)	18.6 (11.9 to 29.1)
Serotype 9N (n=186, 108, 136, 53, 87)	2.3 (2.0 to 2.7)	1.4 (1.1 to 1.7)	5.9 (4.7 to 7.4)	6.8 (4.7 to 9.8)
Serotype 10A (n=200, 111, 148, 71, 93)	4.3 (3.5 to 5.4)	1.0 (0.9 to 1.2)	17.1 (12.7 to 23.0)	11.8 (7.5 to 18.6)
Serotype 11A (n=186, 91, 131, 65, 83)	6.5 (5.2 to 8.2)	1.2 (0.9 to 1.7)	21.0 (14.6 to 30.4)	9.2 (5.9 to 14.4)
Serotype 12F (n=207, 112, 157, 72, 93)	11.8 (9.0 to 15.4)	1.1 (1.0 to 1.3)	82.2 (62.9 to 107.4)	41.9 (26.1 to 67.2)
Serotype 15A (n=142, 78, 110, 40, 62)	5.6 (4.3 to 7.4)	1.2 (0.9 to 1.5)	9.0 (6.8 to 11.8)	3.0 (2.0 to 4.5)
Serotype 15C (n=197, 108, 141, 68, 82)	8.5 (6.7 to 10.9)	1.3 (1.0 to 1.7)	30.6 (22.5 to 41.5)	12.7 (8.5 to 18.8)
Serotype 16F (n=172, 100, 132, 68, 86)	7.1 (5.9 to 8.5)	1.1 (0.9 to 1.3)	9.8 (7.8 to 12.4)	2.0 (1.5 to 2.7)
Serotype 17F (n=183, 101, 116, 64, 79)	3.7 (3.0 to 4.5)	0.9 (0.8 to 1.1)	13.5 (9.5 to 19.2)	8.1 (5.6 to 11.7)
Serotype 20A (n=184, 105, 129, 69, 81)	3.7 (3.0 to 4.5)	0.9 (0.8 to 1.0)	12.2 (9.3 to 16.0)	6.0 (4.4 to 8.3)
Serotype 23A (n=157, 76, 118, 38, 65)	8.4 (6.2 to 11.6)	1.4 (1.0 to 1.9)	19.0 (13.5 to 26.9)	2.5 (1.3 to 4.9)
Serotype 23B (n=191, 109, 155, 71, 94)	21.4 (16.2 to 28.1)	4.2 (2.9 to 6.0)	35.5 (25.9 to 48.6)	5.2 (3.5 to 7.6)
Serotype 24F (n=187, 91, 127, 61, 82)	25.8 (19.5 to 34.0)	1.0 (0.8 to 1.3)	31.1 (22.8 to 42.6)	0.9 (0.7 to 1.3)
Serotype 31 (n=179, 97, 134, 61, 84)	16.7 (12.5 to 22.3)	0.9 (0.7 to 1.2)	35.6 (24.8 to 51.2)	1.7 (1.1 to 2.6)
Serotype 35B (n=183, 106, 144, 71, 85)	6.0 (4.8 to 7.4)	1.0 (0.8 to 1.2)	7.2 (5.6 to 9.2)	1.4 (1.1 to 1.8)

End point values	Cohort 3: V116			

Subject group type	Reporting group			
Number of subjects analysed	98			
Units: Ratio				
geometric mean (confidence interval 95%)				
Serotype 3 (n=164, 91, 131, 68, 76)	5.0 (3.6 to 7.0)			
Serotype 6A (n=171, 87, 136, 66, 89)	5.5 (4.1 to 7.4)			
Serotype 7F (n=200, 102, 146, 69, 92)	3.9 (2.9 to 5.3)			
Serotype 19A (n=194, 104, 149, 72, 90)	2.5 (1.8 to 3.3)			
Serotype 22F (n=193, 102, 124, 64, 94)	7.5 (4.9 to 11.4)			
Serotype 33F (n=177, 93, 125, 50, 85)	2.7 (2.0 to 3.7)			
Serotype 8 (n=198, 108, 151, 71, 96)	3.8 (2.7 to 5.3)			
Serotype 9N (n=186, 108, 136, 53, 87)	3.5 (2.7 to 4.5)			
Serotype 10A (n=200, 111, 148, 71, 93)	4.7 (3.4 to 6.5)			
Serotype 11A (n=186, 91, 131, 65, 83)	9.5 (6.2 to 14.4)			
Serotype 12F (n=207, 112, 157, 72, 93)	13.7 (9.0 to 20.8)			
Serotype 15A (n=142, 78, 110, 40, 62)	7.2 (4.6 to 11.2)			
Serotype 15C (n=197, 108, 141, 68, 82)	11.6 (8.1 to 16.4)			
Serotype 16F (n=172, 100, 132, 68, 86)	7.2 (5.5 to 9.6)			
Serotype 17F (n=183, 101, 116, 64, 79)	6.5 (4.6 to 9.3)			
Serotype 20A (n=184, 105, 129, 69, 81)	4.4 (3.1 to 6.1)			
Serotype 23A (n=157, 76, 118, 38, 65)	16.3 (10.3 to 25.7)			
Serotype 23B (n=191, 109, 155, 71, 94)	26.1 (17.5 to 38.9)			
Serotype 24F (n=187, 91, 127, 61, 82)	39.5 (27.4 to 56.9)			
Serotype 31 (n=179, 97, 134, 61, 84)	30.5 (19.1 to 48.6)			
Serotype 35B (n=183, 106, 144, 71, 85)	5.7 (4.2 to 7.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Achieve a ≥4-fold Increase in Serotype-specific OPA Responses

End point title	Percentage of Participants Who Achieve a ≥4-fold Increase in Serotype-specific OPA Responses

End point description:

Activity for the serotypes contained in V116 was determined using a MOPA. The percentage of participants with a ≥4-fold rise from baseline to at 30 days post-vaccination for OPA responses with 95% confidence intervals are presented. 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 1 (Baseline) and 30 days post-vaccination

End point values	Cohort 1: V116	Cohort 1: PCV15	Cohort 2: V116	Cohort 2: PPSV23
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	212	115	164	76
Units: Percentage of Participants				
number (confidence interval 95%)				
Serotype 3 (n=164, 91, 131, 68, 76)	54.9 (46.9 to 62.6)	54.9 (44.2 to 65.4)	64.1 (55.3 to 72.3)	66.2 (53.7 to 77.2)
Serotype 6A (n=171, 87, 136, 66, 89)	57.9 (50.1 to 65.4)	58.6 (47.6 to 69.1)	46.3 (37.7 to 55.1)	18.2 (9.8 to 29.6)
Serotype 7F (n=200, 102, 146, 69, 92)	38.5 (31.7 to 45.6)	43.1 (33.4 to 53.3)	44.5 (36.3 to 53.0)	49.3 (37.0 to 61.6)
Serotype 19A (n=194, 104, 149, 72, 90)	28.4 (22.1 to 35.2)	34.6 (25.6 to 44.6)	33.6 (26.0 to 41.7)	38.9 (27.6 to 51.1)
Serotype 22F (n=193, 102, 124, 64, 94)	53.9 (46.6 to 61.1)	54.9 (44.7 to 64.8)	77.4 (69.0 to 84.4)	65.6 (52.7 to 77.1)
Serotype 33F (n=177, 93, 125, 50, 85)	19.8 (14.2 to 26.4)	19.4 (11.9 to 28.9)	52.0 (42.9 to 61.0)	56.0 (41.3 to 70.0)
Serotype 8 (n=198, 108, 151, 71, 96)	33.3 (26.8 to 40.4)	2.8 (0.6 to 7.9)	70.2 (62.2 to 77.4)	74.6 (62.9 to 84.2)
Serotype 9N (n=186, 108, 136, 53, 87)	22.0 (16.3 to 28.7)	6.5 (2.6 to 12.9)	57.4 (48.6 to 65.8)	67.9 (53.7 to 80.1)
Serotype 10A (n=200, 111, 148, 71, 93)	46.0 (38.9 to 53.2)	2.7 (0.6 to 7.7)	74.3 (66.5 to 81.1)	67.6 (55.5 to 78.2)
Serotype 11A (n=186, 91, 131, 65, 83)	53.8 (46.3 to 61.1)	12.1 (6.2 to 20.6)	73.3 (64.8 to 80.6)	53.8 (41.0 to 66.3)
Serotype 12F (n=207, 112, 157, 72, 93)	62.8 (55.8 to 69.4)	6.3 (2.5 to 12.5)	93.0 (87.8 to 96.5)	81.9 (71.1 to 90.0)
Serotype 15A (n=142, 78, 110, 40, 62)	53.5 (45.0 to 61.9)	12.8 (6.3 to 22.3)	70.9 (61.5 to 79.2)	35.0 (20.6 to 51.7)
Serotype 15C (n=197, 108, 141, 68, 82)	61.4 (54.2 to 68.3)	10.2 (5.2 to 17.5)	84.4 (77.3 to 90.0)	72.1 (59.9 to 82.3)
Serotype 16F (n=172, 100, 132, 68, 86)	68.0 (60.5 to 74.9)	8.0 (3.5 to 15.2)	70.5 (61.9 to 78.1)	30.9 (20.2 to 43.3)
Serotype 17F (n=183, 101, 116, 64, 79)	37.7 (30.7 to 45.2)	2.0 (0.2 to 7.0)	74.1 (65.2 to 81.8)	62.5 (49.5 to 74.3)
Serotype 20A (n=184, 105, 129, 69, 81	37.5 (30.5 to 44.9)	2.9 (0.6 to 8.1)	76.7 (68.5 to 83.7)	60.9 (48.4 to 72.4)
Serotype 23A (n=157, 76, 118, 38, 65)	59.9 (51.8 to 67.6)	21.1 (12.5 to 31.9)	73.7 (64.8 to 81.4)	34.2 (19.6 to 51.4)
Serotype 23B (n=191, 109, 155, 71, 94)	74.9 (68.1 to 80.9)	40.4 (31.1 to 50.2)	80.6 (73.5 to 86.5)	43.7 (31.9 to 56.0)
Serotype 24F (n=187, 91, 127, 61, 82)	80.2 (73.8 to 85.7)	7.7 (3.1 to 15.2)	81.9 (74.1 to 88.2)	4.9 (1.0 to 13.7)
Serotype 31 (n=179, 97, 134, 61, 84)	70.9 (63.7 to 77.5)	8.2 (3.6 to 15.6)	81.3 (73.7 to 87.5)	18.0 (9.4 to 30.0)
Serotype 35B (n=183, 106, 144, 71, 85)	55.2 (47.7 to 62.5)	7.5 (3.3 to 14.3)	65.3 (56.9 to 73.0)	7.0 (2.3 to 15.7)

End point values	Cohort 3: V116			

Subject group type	Reporting group			
Number of subjects analysed	98			
Units: Percentage of Participants				
number (confidence interval 95%)				
Serotype 3 (n=164, 91, 131, 68, 76)	48.7 (37.0 to 60.4)			
Serotype 6A (n=171, 87, 136, 66, 89)	56.2 (45.3 to 66.7)			
Serotype 7F (n=200, 102, 146, 69, 92)	38.0 (28.1 to 48.8)			
Serotype 19A (n=194, 104, 149, 72, 90)	30.0 (20.8 to 40.6)			
Serotype 22F (n=193, 102, 124, 64, 94)	50.0 (39.5 to 60.5)			
Serotype 33F (n=177, 93, 125, 50, 85)	29.4 (20.0 to 40.3)			
Serotype 8 (n=198, 108, 151, 71, 96)	34.4 (25.0 to 44.8)			
Serotype 9N (n=186, 108, 136, 53, 87)	39.1 (28.8 to 50.1)			
Serotype 10A (n=200, 111, 148, 71, 93)	49.5 (38.9 to 60.0)			
Serotype 11A (n=186, 91, 131, 65, 83)	59.0 (47.7 to 69.7)			
Serotype 12F (n=207, 112, 157, 72, 93)	60.2 (49.5 to 70.2)			
Serotype 15A (n=142, 78, 110, 40, 62)	59.7 (46.4 to 71.9)			
Serotype 15C (n=197, 108, 141, 68, 82)	72.0 (60.9 to 81.3)			
Serotype 16F (n=172, 100, 132, 68, 86)	70.9 (60.1 to 80.2)			
Serotype 17F (n=183, 101, 116, 64, 79)	54.4 (42.8 to 65.7)			
Serotype 20A (n=184, 105, 129, 69, 81	46.9 (35.7 to 58.3)			
Serotype 23A (n=157, 76, 118, 38, 65)	80.0 (68.2 to 88.9)			
Serotype 23B (n=191, 109, 155, 71, 94)	80.9 (71.4 to 88.2)			
Serotype 24F (n=187, 91, 127, 61, 82)	89.0 (80.2 to 94.9)			
Serotype 31 (n=179, 97, 134, 61, 84)	82.1 (72.3 to 89.6)			
Serotype 35B (n=183, 106, 144, 71, 85)	57.6 (46.4 to 68.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Fold Rise of Serotype-specific IgG

End point title	Geometric Mean Fold Rise of Serotype-specific IgG

End point description:

Activity for the serotypes contained in V116 was determined using a PnECL assay. Geometric mean fold rise (GMFR) is defined as the geometric mean of the ratio of concentration at Day 30 after vaccination divided by concentration at baseline. The GMFRs IgG responses from baseline to 30 days post-

vaccination with 95% confidence intervals are presented. 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 1 (Baseline) and 30 days post-vaccination

End point values	Cohort 1: V116	Cohort 1: PCV15	Cohort 2: V116	Cohort 2: PPSV23
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	220	117	167	81
Units: Ratio				
geometric mean (confidence interval 95%)				
Serotype 3 (n=220, 117, 167, 81, 99)	3.6 (3.2 to 4.0)	3.1 (2.6 to 3.7)	3.7 (3.2 to 4.3)	5.7 (4.3 to 7.4)
Serotype 6A (n=219, 117, 167, 81, 99)	5.9 (5.0 to 7.1)	8.0 (6.1 to 10.6)	3.3 (2.7 to 4.0)	2.5 (1.9 to 3.2)
Serotype 7F (n=219, 117, 167, 81, 99)	3.3 (2.8 to 3.8)	2.9 (2.3 to 3.5)	3.2 (2.7 to 3.8)	3.2 (2.6 to 3.9)
Serotype 19A (n=219, 117, 167, 81, 99)	2.3 (2.0 to 2.7)	3.4 (2.8 to 4.2)	2.2 (1.9 to 2.5)	3.0 (2.4 to 3.6)
Serotype 22F (n=219, 117, 167, 81, 99)	4.2 (3.6 to 4.9)	3.4 (2.8 to 4.2)	14.3 (11.4 to 18.0)	8.5 (6.2 to 11.6)
Serotype 33F (n=220, 117, 167, 81, 99)	2.2 (1.9 to 2.5)	1.8 (1.5 to 2.1)	8.6 (7.1 to 10.5)	10.5 (7.9 to 13.9)
Serotype 8 (n=220, 117, 167, 81, 99)	2.7 (2.4 to 3.1)	1.0 (0.9 to 1.1)	12.1 (9.8 to 15.0)	14.4 (10.3 to 20.0)
Serotype 9N (n=217, 117, 167, 81, 99)	2.9 (2.4 to 3.4)	1.4 (1.2 to 1.6)	8.7 (7.1 to 10.6)	9.1 (6.8 to 12.1)
Serotype 10A (n=220, 117, 167, 81, 99)	4.4 (3.7 to 5.2)	1.0 (0.9 to 1.0)	18.9 (15.3 to 23.4)	10.1 (7.6 to 13.4)
Serotype 11A (n=219, 117, 167, 81, 99)	4.1 (3.6 to 4.7)	1.0 (0.9 to 1.0)	10.3 (8.5 to 12.6)	5.6 (4.4 to 7.2)
Serotype 12F (n=220, 117, 167, 81, 99)	4.2 (3.6 to 5.0)	1.0 (0.9 to 1.1)	14.2 (11.3 to 17.9)	8.4 (5.8 to 12.0)
Serotype 15A (n=220, 117, 167, 81, 99)	12.2 (10.1 to 14.7)	1.0 (0.9 to 1.1)	24.5 (19.7 to 30.3)	2.4 (2.0 to 3.0)
Serotype 15C (n=219, 117, 166, 81, 99)	5.8 (4.9 to 6.9)	1.0 (0.9 to 1.2)	18.8 (14.9 to 23.8)	6.2 (4.8 to 8.2)
Serotype 16F (n=218, 117, 166, 81, 99)	15.2 (12.7 to 18.2)	1.1 (1.0 to 1.2)	15.7 (12.9 to 19.0)	1.6 (1.3 to 1.8)
Serotype 17F (n=219, 117, 167, 81, 99)	4.7 (4.0 to 5.5)	1.0 (0.9 to 1.1)	17.4 (14.3 to 21.1)	10.5 (7.8 to 14.1)
Serotype 20A (n=219, 117, 167, 81, 99)	3.8 (3.3 to 4.4)	1.0 (0.9 to 1.1)	14.8 (12.2 to 17.9)	8.5 (6.4 to 11.4)
Serotype 23A (n=219, 117, 167, 81, 99)	13.5 (11.1 to 16.5)	1.8 (1.5 to 2.2)	18.9 (15.3 to 23.4)	2.3 (1.9 to 2.7)
Serotype 23B (n=219, 117, 167, 81, 99)	8.2 (6.7 to 10.0)	2.7 (2.1 to 3.5)	7.3 (6.0 to 8.9)	2.3 (1.9 to 2.9)
Serotype 24F (n=219, 117, 167, 81, 99)	26.9 (21.8 to 33.1)	1.0 (0.9 to 1.1)	21.7 (17.3 to 27.2)	1.0 (0.9 to 1.1)
Serotype 31 (n=217, 117, 167, 81, 90)	13.1 (11.0 to 15.6)	1.1 (1.0 to 1.2)	14.4 (11.9 to 17.3)	1.5 (1.3 to 1.8)
Serotype 35B (n=218, 117, 167, 81, 99)	16.8 (13.9 to 20.3)	1.0 (0.9 to 1.0)	15.6 (12.9 to 18.7)	0.9 (0.9 to 1.0)

End point values	Cohort 3: V116			
Subject group type	Reporting group			
Number of subjects analysed	99			
Units: Ratio				
geometric mean (confidence interval 95%)				
Serotype 3 (n=220, 117, 167, 81, 99)	2.9 (2.3 to 3.5)			
Serotype 6A (n=219, 117, 167, 81, 99)	4.4 (3.4 to 5.7)			
Serotype 7F (n=219, 117, 167, 81, 99)	3.2 (2.6 to 4.0)			
Serotype 19A (n=219, 117, 167, 81, 99)	2.0 (1.7 to 2.4)			
Serotype 22F (n=219, 117, 167, 81, 99)	3.5 (2.7 to 4.6)			
Serotype 33F (n=220, 117, 167, 81, 99)	2.4 (1.9 to 3.0)			
Serotype 8 (n=220, 117, 167, 81, 99)	2.3 (1.9 to 2.8)			
Serotype 9N (n=217, 117, 167, 81, 99)	3.2 (2.6 to 3.9)			
Serotype 10A (n=220, 117, 167, 81, 99)	4.2 (3.1 to 5.5)			
Serotype 11A (n=219, 117, 167, 81, 99)	3.5 (2.7 to 4.3)			
Serotype 12F (n=220, 117, 167, 81, 99)	3.5 (2.7 to 4.5)			
Serotype 15A (n=220, 117, 167, 81, 99)	16.6 (12.0 to 22.9)			
Serotype 15C (n=219, 117, 166, 81, 99)	6.4 (5.0 to 8.1)			
Serotype 16F (n=218, 117, 166, 81, 99)	11.9 (9.2 to 15.4)			
Serotype 17F (n=219, 117, 167, 81, 99)	3.8 (2.9 to 5.0)			
Serotype 20A (n=219, 117, 167, 81, 99)	3.7 (2.9 to 4.8)			
Serotype 23A (n=219, 117, 167, 81, 99)	13.1 (9.6 to 17.7)			
Serotype 23B (n=219, 117, 167, 81, 99)	7.3 (5.4 to 9.7)			
Serotype 24F (n=219, 117, 167, 81, 99)	24.4 (17.1 to 34.9)			
Serotype 31 (n=217, 117, 167, 81, 90)	13.0 (9.9 to 17.0)			
Serotype 35B (n=218, 117, 167, 81, 99)	15.7 (11.9 to 20.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Achieve a ≥4-fold Increase in Serotype-specific IgG Response

End point title	Percentage of Participants Who Achieve a ≥4-fold Increase in Serotype-specific IgG Response

End point description:

Activity for the serotypes contained in V116 was determined using a PnECL assay. The percentage of

participants with a ≥4-fold rise from baseline to at 30 days post-vaccination for IgG responses with 95% confidence intervals are presented. 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 1 (Baseline) and 30 days post-vaccination

End point values	Cohort 1: V116	Cohort 1: PCV15	Cohort 2: V116	Cohort 2: PPSV23
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	220	117	167	81
Units: Percentage of Participants				
number (confidence interval 95%)				
Serotype 3 (n=220, 117, 167, 81, 99)	42.7 (36.1 to 49.6)	36.8 (28.0 to 46.2)	40.7 (33.2 to 48.6)	54.3 (42.9 to 65.4)
Serotype 6A (n=219, 117, 167, 81, 99)	56.2 (49.3 to 62.8)	65.0 (55.6 to 73.5)	35.9 (28.7 to 43.7)	27.2 (17.9 to 38.2)
Serotype 7F (n=219, 117, 167, 81, 99)	34.7 (28.4 to 41.4)	29.9 (21.8 to 39.1)	37.7 (30.4 to 45.5)	33.3 (23.2 to 44.7)
Serotype 19A (n=219, 117, 167, 81, 99)	24.7 (19.1 to 30.9)	37.6 (28.8 to 47.0)	19.8 (14.0 to 26.6)	33.3 (23.2 to 44.7)
Serotype 22F (n=219, 117, 167, 81, 99)	39.3 (32.8 to 46.1)	35.0 (26.5 to 44.4)	78.4 (71.4 to 84.4)	65.4 (54.0 to 75.7)
Serotype 33F (n=220, 117, 167, 81, 99)	19.1 (14.1 to 24.9)	12.8 (7.4 to 20.3)	72.5 (65.0 to 79.1)	75.3 (64.5 to 84.2)
Serotype 8 (n=220, 117, 167, 81, 99)	29.5 (23.6 to 36.0)	0.9 (0.0 to 4.7)	78.4 (71.4 to 84.4)	76.5 (65.8 to 85.2)
Serotype 9N (n=217, 117, 167, 81, 99)	31.8 (25.7 to 38.4)	7.7 (3.6 to 14.1)	68.9 (61.2 to 75.8)	72.8 (61.8 to 82.1)
Serotype 10A (n=220, 117, 167, 81, 99)	45.5 (38.7 to 52.3)	0.9 (0.0 to 4.7)	82.6 (76.0 to 88.1)	80.2 (69.9 to 88.3)
Serotype 11A (n=219, 117, 167, 81, 99)	43.8 (37.2 to 50.7)	0.0 (0.0 to 3.1)	72.5 (65.0 to 79.1)	63.0 (51.5 to 73.4)
Serotype 12F (n=220, 117, 167, 81, 99)	44.5 (37.9 to 51.4)	2.6 (0.5 to 7.3)	75.4 (68.2 to 81.8)	60.5 (49.0 to 71.2)
Serotype 15A (n=220, 117, 167, 81, 99)	73.6 (67.3 to 79.3)	0.9 (0.0 to 4.7)	89.8 (84.2 to 94.0)	28.4 (18.9 to 39.5)
Serotype 15C (n=219, 117, 166, 81, 99)	57.5 (50.7 to 64.2)	3.4 (0.9 to 8.5)	80.1 (73.2 to 85.9)	64.2 (52.8 to 74.6)
Serotype 16F (n=218, 117, 166, 81, 99)	82.1 (76.4 to 87.0)	2.6 (0.5 to 7.3)	84.9 (78.6 to 90.0)	13.6 (7.0 to 23.0)
Serotype 17F (n=219, 117, 167, 81, 99)	48.9 (42.1 to 55.7)	1.7 (0.2 to 6.0)	83.8 (77.4 to 89.1)	74.1 (63.1 to 83.2)
Serotype 20A (n=219, 117, 167, 81, 99)	36.5 (30.1 to 43.3)	0.9 (0.0 to 4.7)	83.2 (76.7 to 88.6)	69.1 (57.9 to 78.9)
Serotype 23A (n=219, 117, 166, 81, 99)	77.6 (71.5 to 83.0)	17.1 (10.8 to 25.2)	86.7 (80.6 to 91.5)	21.0 (12.7 to 31.5)
Serotype 23B (n=219, 117, 167, 81, 99)	64.8 (58.1 to 71.2)	26.5 (18.8 to 35.5)	60.5 (52.6 to 67.9)	21.0 (12.7 to 31.5)
Serotype 24F (n=219, 117, 167, 81, 99)	85.4 (80.0 to 89.8)	0.0 (0.0 to 3.1)	88.0 (82.1 to 92.5)	0.0 (0.0 to 4.5)
Serotype 31 (n=217, 117, 167, 81, 99)	79.7 (73.8 to 84.9)	2.6 (0.5 to 7.3)	84.4 (78.0 to 89.6)	11.1 (5.2 to 20.0)
Serotype 35B (n=218, 117, 167, 81, 99)	83.9 (78.4 to 88.6)	0.0 (0.0 to 3.1)	82.6 (76.0 to 88.1)	0.0 (0.0 to 4.5)

End point values	Cohort 3: V116			
Subject group type	Reporting group			
Number of subjects analysed	99			
Units: Percentage of Participants				
number (confidence interval 95%)				
Serotype 3 (n=220, 117, 167, 81, 99)	35.4 (26.0 to 45.6)			
Serotype 6A (n=219, 117, 167, 81, 99)	45.5 (35.4 to 55.8)			
Serotype 7F (n=219, 117, 167, 81, 99)	37.4 (27.9 to 47.7)			
Serotype 19A (n=219, 117, 167, 81, 99)	19.2 (12.0 to 28.3)			
Serotype 22F (n=219, 117, 167, 81, 99)	43.4 (33.5 to 53.8)			
Serotype 33F (n=220, 117, 167, 81, 99)	27.3 (18.8 to 37.1)			
Serotype 8 (n=220, 117, 167, 81, 99)	26.3 (17.9 to 36.1)			
Serotype 9N (n=217, 117, 167, 81, 99)	36.4 (26.9 to 46.6)			
Serotype 10A (n=220, 117, 167, 81, 99)	46.5 (36.4 to 56.8)			
Serotype 11A (n=219, 117, 167, 81, 99)	43.4 (33.5 to 53.8)			
Serotype 12F (n=220, 117, 167, 81, 99)	39.4 (29.7 to 49.7)			
Serotype 15A (n=220, 117, 167, 81, 99)	77.8 (68.3 to 85.5)			
Serotype 15C (n=219, 117, 166, 81, 99)	66.7 (56.5 to 75.8)			
Serotype 16F (n=218, 117, 166, 81, 99)	77.8 (68.3 to 85.5)			
Serotype 17F (n=219, 117, 167, 81, 99)	44.4 (34.5 to 54.8)			
Serotype 20A (n=219, 117, 167, 81, 99)	49.5 (39.3 to 59.7)			
Serotype 23A (n=219, 117, 166, 81, 99)	77.8 (68.3 to 85.5)			
Serotype 23B (n=219, 117, 167, 81, 99)	64.6 (54.4 to 74.0)			
Serotype 24F (n=219, 117, 167, 81, 99)	83.8 (75.1 to 90.5)			
Serotype 31 (n=217, 117, 167, 81, 99)	80.8 (71.7 to 88.0)			
Serotype 35B (n=218, 117, 167, 81, 99)	84.8 (76.2 to 91.3)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to approximately 30 days post-vaccination for non-serious adverse events (AEs) and up to approximately 180 days for serious AEs and deaths.

Adverse event reporting additional description:

The analysis population for deaths (all-causes) included all randomized participants (N=231, N=119, N=176, N=85, N=106). The analysis population for AEs included all randomized participants who received the study vaccination.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups

Reporting group title	Cohort 1: V116
Reporting group description: -	
Reporting group title	Cohort 1: PCV15
Reporting group description: -	
Reporting group title	Cohort 2: V116
Reporting group description: -	
Reporting group title	Cohort 2: PPSV23
Reporting group description: -	
Reporting group title	Cohort 3: V116

Reporting group description: -

Serious adverse events	Cohort 1: V116	Cohort 1: PCV15	Cohort 2: V116
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 230 (0.87%)	4 / 117 (3.42%)	2 / 174 (1.15%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 230 (0.00%)	1 / 117 (0.85%)	0 / 174 (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
Cardiac disorders			
Cardiac failure congestive			
subjects affected / exposed	1 / 230 (0.43%)	0 / 117 (0.00%)	0 / 174 (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
Cardiac failure			

subjects affected / exposed	0 / 230 (0.00%)	1 / 117 (0.85%)	0 / 174 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial ischaemia			
subjects affected / exposed	0 / 230 (0.00%)	1 / 117 (0.85%)	0 / 174 (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
Nervous system disorders			
Ischaemic stroke			
subjects affected / exposed	0 / 230 (0.00%)	0 / 117 (0.00%)	0 / 174 (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
Gastrointestinal disorders			
Anal fissure			
subjects affected / exposed	0 / 230 (0.00%)	0 / 117 (0.00%)	1 / 174 (0.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortoenteric fistula			
subjects affected / exposed	0 / 230 (0.00%)	1 / 117 (0.85%)	0 / 174 (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
Small intestinal perforation			
subjects affected / exposed	0 / 230 (0.00%)	1 / 117 (0.85%)	0 / 174 (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
Mallory-Weiss syndrome			
subjects affected / exposed	0 / 230 (0.00%)	1 / 117 (0.85%)	0 / 174 (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
Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	0 / 230 (0.00%)	0 / 117 (0.00%)	0 / 174 (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

Cholelithiasis			
subjects affected / exposed	0 / 230 (0.00%)	0 / 117 (0.00%)	0 / 174 (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			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 230 (0.00%)	0 / 117 (0.00%)	1 / 174 (0.57%)
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			
Injection site cellulitis			
subjects affected / exposed	1 / 230 (0.43%)	0 / 117 (0.00%)	0 / 174 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 230 (0.00%)	1 / 117 (0.85%)	0 / 174 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 230 (0.00%)	0 / 117 (0.00%)	0 / 174 (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	Cohort 2: PPSV23	Cohort 3: V116	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 85 (3.53%)	2 / 105 (1.90%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 85 (0.00%)	0 / 105 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac failure congestive			

subjects affected / exposed	0 / 85 (0.00%)	0 / 105 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	0 / 85 (0.00%)	0 / 105 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial ischaemia			
subjects affected / exposed	0 / 85 (0.00%)	0 / 105 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Ischaemic stroke			
subjects affected / exposed	1 / 85 (1.18%)	0 / 105 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Anal fissure			
subjects affected / exposed	0 / 85 (0.00%)	0 / 105 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortoenteric fistula			
subjects affected / exposed	0 / 85 (0.00%)	0 / 105 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal perforation			
subjects affected / exposed	0 / 85 (0.00%)	0 / 105 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mallory-Weiss syndrome			
subjects affected / exposed	0 / 85 (0.00%)	0 / 105 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			

Cholangitis			
subjects affected / exposed	1 / 85 (1.18%)	0 / 105 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	0 / 85 (0.00%)	1 / 105 (0.95%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 85 (1.18%)	0 / 105 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Injection site cellulitis			
subjects affected / exposed	0 / 85 (0.00%)	0 / 105 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 85 (0.00%)	0 / 105 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 85 (0.00%)	1 / 105 (0.95%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Cohort 1: V116	Cohort 1: PCV15	Cohort 2: V116
Total subjects affected by non-serious adverse events			
subjects affected / exposed	107 / 230 (46.52%)	66 / 117 (56.41%)	85 / 174 (48.85%)
Nervous system disorders			

Headache			
subjects affected / exposed	17 / 230 (7.39%)	11 / 117 (9.40%)	18 / 174 (10.34%)
occurrences (all)	17	11	19
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	33 / 230 (14.35%)	20 / 117 (17.09%)	33 / 174 (18.97%)
occurrences (all)	33	20	34
Injection site erythema			
subjects affected / exposed	19 / 230 (8.26%)	9 / 117 (7.69%)	14 / 174 (8.05%)
occurrences (all)	19	9	14
Injection site pain			
subjects affected / exposed	82 / 230 (35.65%)	51 / 117 (43.59%)	72 / 174 (41.38%)
occurrences (all)	82	51	72
Injection site swelling			
subjects affected / exposed	20 / 230 (8.70%)	10 / 117 (8.55%)	8 / 174 (4.60%)
occurrences (all)	20	10	8
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	17 / 230 (7.39%)	5 / 117 (4.27%)	17 / 174 (9.77%)
occurrences (all)	17	5	17

Non-serious adverse events	Cohort 2: PPSV23	Cohort 3: V116	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	52 / 85 (61.18%)	51 / 105 (48.57%)	
Nervous system disorders			
Headache			
subjects affected / exposed	10 / 85 (11.76%)	9 / 105 (8.57%)	
occurrences (all)	10	9	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	12 / 85 (14.12%)	23 / 105 (21.90%)	
occurrences (all)	12	23	
Injection site erythema			
subjects affected / exposed	8 / 85 (9.41%)	8 / 105 (7.62%)	
occurrences (all)	8	8	
Injection site pain			

subjects affected / exposed	40 / 85 (47.06%)	46 / 105 (43.81%)	
occurrences (all)	40	46	
Injection site swelling			
subjects affected / exposed	14 / 85 (16.47%)	11 / 105 (10.48%)	
occurrences (all)	14	11	
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	9 / 85 (10.59%)	9 / 105 (8.57%)	
occurrences (all)	9	9	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 July 2022	Amendment 03: Primary reason for amendment was to revise cohort-specific enrollment restrictions.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported