Clinical trial results:
A Phase 3, Multicenter, Randomized, Double-blind, Active Comparator-controlled Study to Evaluate the Safety, Tolerability, and Immunogenicity of V114 in Healthy Adults 50 Years of Age or Older (PNEU-AGE)

Summary

EudraCT number	2018-004316-22
Trial protocol	ES
Global end of trial date	02 July 2020

Results information

Result version number	v1
This version publication date	10 March 2021
First version publication date	10 March 2021

Trial information

Trial identification

Sponsor protocol code	V114-019

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03950622
WHO universal trial number (UTN)	-
Other trial identifiers	JAPIC-CTI: 194845, Study Acronym: PNEU-AGE

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	30 March 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 March 2020
Global end of trial reached?	Yes
Global end of trial date	02 July 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is 1) to evaluate the safety and tolerability of V114 and 2) to compare the immune responses of the 15 serotypes contained in V114 with V114 versus Prevnar 13™. The primary hypotheses are that 1) V114 is noninferior to Prevnar 13™ as measured by the serotype specific opsonophagocytic activity (OPA) geometric mean titers (GMTs) for 13 shared serotypes at 30 days postvaccination and that 2) V114 is superior to Prevnar 13™ as measured by serotype-specific OPA GMTs for 2 unique serotypes in V114 at 30 days postvaccination.

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	13 June 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	Canada: 188
Country: Number of subjects enrolled	Japan: 245
Country: Number of subjects enrolled	Spain: 100
Country: Number of subjects enrolled	Taiwan: 40
Country: Number of subjects enrolled	United States: 632
Worldwide total number of subjects	1205
EEA total number of subjects	100

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)	374
From 65 to 84 years	826
85 years and over	5

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 1200 participants were planned to be enrolled/randomized.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	V114

Arm description:

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

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

Dosage and administration details:

15-valent pneumococcal conjugate vaccine with serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F, 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.

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

Dosage and administration details:

13-valent pneumococcal conjugate vaccine with serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F in each 0.5 mL dose.

Number of subjects in period 1	V114	Prevnar 13™
Started	604	601
Vaccinated	602	600
Completed	596	594
Not completed	8	7
Adverse event, serious fatal	1	1
Physician decision	1	-
Consent withdrawn by subject	1	-
Protocol Deviation	-	1
Lost to follow-up	5	5

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.	
Reporting group title	Prevnar 13™
Reporting group description:	
Participants received a single 0.5 mL IM injection of Prevnar 13™ on Day 1.	

Reporting group values	V114	Prevnar 13™	Total
Number of subjects	604	601	1205
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)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	187	187	374
From 65-84 years	412	414	826
85 years and over	5	0	5
Age Continuous Units: years			
arithmetic mean	66.2	65.7	
standard deviation	± 7.7	± 7.4	-
Sex: Female, Male Units: Participants			
Female	359	332	691
Male	245	269	514
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	1	1
Asian	150	152	302
Native Hawaiian or Other Pacific Islander	1	0	1
Black or African American	36	37	73
White	410	407	817
More than one race	7	4	11
Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	135	129	264
Not Hispanic or Latino	469	471	940
Unknown or Not Reported	0	1	1

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.	
Reporting group title	Prevnar 13™
Reporting group description:	
Participants received a single 0.5 mL IM injection of Prevnar 13™ on Day 1.	

Primary: Percentage of Participants with a Solicited Injection-site Adverse Event	
End point title	Percentage of Participants with a Solicited Injection-site Adverse Event
End point description:	
An adverse event (AE) is any untoward medical occurrence in a patient or clinical study participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention. Solicited injection-site AEs consist of redness/erythema, swelling, and tenderness/pain. The analysis population included all randomized participants who received study vaccination and were included in the intervention group according to the intervention they received.	
End point type	Primary
End point timeframe:	
Up to Day 5 postvaccination	

End point values	V114	Prevnar 13™		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	602	600		
Units: Percentage of Participants				
number (not applicable)				
Injection site erythema	9.0	11.3		
Injection site pain	54.0	42.3		
Injection site swelling	12.5	11.2		

Statistical analyses

Statistical analysis title	Injection site redness/erythema
Comparison groups	V114 v Prevnar 13™
Number of subjects included in analysis	1202
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.175
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percent
Point estimate	-2.4

Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.8
upper limit	1.1

Statistical analysis title	Injection site tenderness/pain
Comparison groups	V114 v Prevnar 13™
Number of subjects included in analysis	1202
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percent
Point estimate	11.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	6
upper limit	17.2

Statistical analysis title	Injection site swelling
Comparison groups	V114 v Prevnar 13™
Number of subjects included in analysis	1202
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.488
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percent
Point estimate	1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.4
upper limit	5

Primary: Percentage of Participants with Solicited Systemic Adverse Events

End point title	Percentage of Participants with Solicited Systemic Adverse Events

End point description:

An AE is any untoward medical occurrence in a patient or clinical study participant, temporally associated with the use of study treatment, whether or not considered related to the study treatment. Following vaccination with V114 or Prevnar 13™, the percentage of participants with solicited systemic AEs was assessed. The solicited systemic AEs assessed were muscle pain/myalgia, joint pain/arthralgia, headache, and tiredness/fatigue. The analysis population included all randomized participants who

received study vaccination and were included in the intervention group according to the intervention they received.

End point type	Primary
End point timeframe:	
Up to Day 14 postvaccination	

End point values	V114	Prevnar 13™		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	602	600		
Units: Percentage of Participants				
number (not applicable)				
Joint pain/arthralgia	5.3	5.5		
Tiredness/fatigue	17.4	17.3		
Headache	11.6	13.0		
Muscle pain/myalgia	15.4	12.0		

Statistical analyses

Statistical analysis title	Joint pain/arthralgia
Comparison groups	V114 v Prevnar 13™
Number of subjects included in analysis	1202
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.888
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percent
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.8
upper limit	2.4

Statistical analysis title	Tiredness/fatigue
Comparison groups	V114 v Prevnar 13™
Number of subjects included in analysis	1202
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.96
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percent
Point estimate	0.1

Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.2
upper limit	4.4

Statistical analysis title	Headache
Comparison groups	V114 v Prevnar 13™
Number of subjects included in analysis	1202
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.469
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percent
Point estimate	-1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.1
upper limit	2.4

Statistical analysis title	Muscle pain/myalgia
Comparison groups	V114 v Prevnar 13™
Number of subjects included in analysis	1202
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.082
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percent
Point estimate	3.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4
upper limit	7.4

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

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

End point description:

A serious adverse event (SAE) is 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. SAEs that are reported to be at least possibly related by the investigator to study vaccination will be summarized. The analysis population included all randomized participants who

received study vaccination and were included in the intervention group according to the intervention they received.

End point type	Primary

End point timeframe:

Up to Month 6

End point values	V114	Prevnar 13™		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	602	600		
Units: Percentage of Participants				
number (not applicable)	0.0	0.0		

Statistical analyses

Statistical analysis title	Vaccine-related SAEs
Comparison groups	V114 v Prevnar 13™
Number of subjects included in analysis	1202
Analysis specification	Pre-specified
Analysis type	
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percent
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	0.6

Primary: Geometric Mean Titer of Serotype-specific Opsonophagocytic Activity at Day 30

End point title	Geometric Mean Titer of Serotype-specific Opsonophagocytic Activity at Day 30

End point description:

Serotype-specific opsonophagocytic activity (OPA) geometric mean titers (GMTs) (estimated) and GMT ratios with 95% CIs were calculated using a constrained longitudinal data analysis (cLDA) model utilizing data from both vaccination groups. Per the statistical analysis plan, the only CIs calculated were the between-group CIs (for the GMT ratios); within-group CIs were not calculated. OPA for the serotypes contained in Prevnar 13™ and V114 (13 serotypes shared with Prevnar 13™ and 2 serotypes unique to V114) were determined using a multiplexed opsonophagocytic assay (MOPA). The analysis population included all randomized participants without protocol deviations, such as failure to receive study vaccine or receipt of prohibited medication prior to study vaccination.

End point type	Primary

End point timeframe:

Day 30

End point values	V114	Prevnar 13™		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	602	600		
Units: Titers				
number (not applicable)				
Serotype 1 (Shared) (n=598, 598)	256.3	322.6		
Serotype 3 (Shared) (n=598, 598)	216.2	135.1		
Serotype 4 (Shared) (n=598, 598)	1125.6	1661.6		
Serotype 5 (Shared) (n=598, 598)	447.3	563.5		
Serotype 6A (Shared) (n=596, 598)	5407.2	5424.5		
Serotype 6B (Shared) (n=598, 598)	4011.7	3258.2		
Serotype 7F (Shared) (n=597, 598)	4617.3	5880.6		
Serotype 9V (Shared) (n=598, 597)	1817.3	2232.9		
Serotype 14 (Shared) (n=598, 598)	1999.3	2656.7		
Serotype 18C (Shared) (n=598, 598)	2757.7	2583.7		
Serotype 19A (Shared) (n=598, 598)	3194.3	3979.8		
Serotype 19F (Shared) (n=598, 598)	1695.1	1917.8		
Serotype 23F (Shared) (n=598, 598)	2045.4	1740.4		
Serotype 22F (Unique to V114) (n=598, 598)	2375.2	74.6		
Serotype 33F (Unique to V114) (n=598, 598)	7994.7	1124.9		

Statistical analyses

Statistical analysis title	Serotype 1 (Shared)
Comparison groups	V114 v Prevnar 13™
Number of subjects included in analysis	1202
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	cLDA
Parameter estimate	GMT Ratio
Point estimate	0.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.66
upper limit	0.96

Statistical analysis title	Serotype 3 (Shared)
Comparison groups	V114 v Prevnar 13™

Number of subjects included in analysis	1202
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	cLDA
Parameter estimate	GMT Ratio
Point estimate	1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.38
upper limit	1.85

Statistical analysis title	Serotype 4 (Shared)
Comparison groups	V114 v Prevnar 13™
Number of subjects included in analysis	1202
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	cLDA
Parameter estimate	GMT Ratio
Point estimate	0.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.57
upper limit	0.8

Statistical analysis title	Serotype 5 (Shared)
Comparison groups	V114 v Prevnar 13™
Number of subjects included in analysis	1202
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	cLDA
Parameter estimate	GMT Ratio
Point estimate	0.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.64
upper limit	0.98

Statistical analysis title	Serotype 6A (Shared)

Comparison groups	V114 v Prevnar 13™
Number of subjects included in analysis	1202
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	cLDA
Parameter estimate	GMT Ratio
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.84
upper limit	1.19

Statistical analysis title	Serotype 6B (Shared)
Comparison groups	V114 v Prevnar 13™
Number of subjects included in analysis	1202
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	cLDA
Parameter estimate	GMT Ratio
Point estimate	1.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.02
upper limit	1.48

Statistical analysis title	Serotype 7F (Shared)
Comparison groups	V114 v Prevnar 13™
Number of subjects included in analysis	1202
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	cLDA
Parameter estimate	GMT Ratio
Point estimate	0.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.68
upper limit	0.9

Statistical analysis title	Serotype 9V (Shared)
Comparison groups	V114 v Prevnar 13™
Number of subjects included in analysis	1202
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	cLDA
Parameter estimate	GMT Ratio
Point estimate	0.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	0.94

Statistical analysis title	Serotype 14 (Shared)
Comparison groups	V114 v Prevnar 13™
Number of subjects included in analysis	1202
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	cLDA
Parameter estimate	GMT Ratio
Point estimate	0.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.64
upper limit	0.89

Statistical analysis title	Serotype 18C (Shared)
Comparison groups	V114 v Prevnar 13™
Number of subjects included in analysis	1202
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	cLDA
Parameter estimate	GMT Ratio
Point estimate	1.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.91
upper limit	1.26

Statistical analysis title	Serotype 19A (Shared)
Comparison groups	V114 v Prevnar 13™
Number of subjects included in analysis	1202
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	cLDA
Parameter estimate	GMT Ratio
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	0.93

Statistical analysis title	Serotype 19F (Shared)
Comparison groups	V114 v Prevnar 13™
Number of subjects included in analysis	1202
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	cLDA
Parameter estimate	GMT Ratio
Point estimate	0.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.76
upper limit	1.02

Statistical analysis title	Serotype 23F (Shared)
Comparison groups	V114 v Prevnar 13™
Number of subjects included in analysis	1202
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	cLDA
Parameter estimate	GMT Ratio
Point estimate	1.18

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.96
upper limit	1.44

Statistical analysis title	Serotype 22F (Unique to V114)
Comparison groups	V114 v Prevnar 13™
Number of subjects included in analysis	1202
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	cLDA
Parameter estimate	GMT Ratio
Point estimate	31.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	25.35
upper limit	39.97

Statistical analysis title	Serotype 33F (Unique to V114)
Comparison groups	V114 v Prevnar 13™
Number of subjects included in analysis	1202
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	cLDA
Parameter estimate	GMT Ratio
Point estimate	7.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.07
upper limit	8.32

Primary: Percentage of Participants with ≥4-Fold Rise in Serotype-specific OPA for 2 Unique V114 Serotypes

End point title	Percentage of Participants with ≥4-Fold Rise in Serotype-specific OPA for 2 Unique V114 Serotypes

End point description:

Activity for the serotypes contained in Prevnar 13™ and V114 was determined using a multiplexed opsonophagocytic assay (MOPA). The percentage of participants who had ≥4-fold rise in OPA titers were calculated from baseline (Day 1) to 30 days postvaccination (Day 30) for OPA responses for the 2 unique serotypes in V114. The observed response percentage (m/n) included: m=the number of

participants with the indicated response divided by n=the number of participants contributing to the analysis. Per the statistical analysis plan, the only CIs calculated were the between-group CIs (for the percentage point difference); within-group CIs were not calculated.

End point type	Primary
End point timeframe:	
Day 1 (Baseline) and Day 30	

End point values	V114	Prevnar 13™		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	602	600		
Units: Percentage of Participants				
number (not applicable)				
Serotype 22F (Unique to V114) (n=524, 498)	71.4	14.3		
Serotype 33F (Unique to V114)(n=578, 560)	56.7	6.3		

Statistical analyses

Statistical analysis title	Serotype 22F (Unique to V114)
Comparison groups	V114 v Prevnar 13™
Number of subjects included in analysis	1202
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Percentage Point Difference
Point estimate	57.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	52
upper limit	61.8

Statistical analysis title	Serotype 33F (Unique to V114)
Comparison groups	V114 v Prevnar 13™
Number of subjects included in analysis	1202
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Percentage Point Difference
Point estimate	50.5

Confidence interval	
level	95 %
sides	2-sided
lower limit	45.9
upper limit	54.9

Secondary: GMT of Serotype-specific OPA for Serotype 3 at Day 30

End point title	GMT of Serotype-specific OPA for Serotype 3 at Day 30

End point description:

Serotype-specific OPA GMTs (estimated) and GMT ratios with 95% CIs were calculated using a cLDA model utilizing data from both vaccination groups. Per the statistical analysis plan, the only CIs calculated were the between-group CIs (for the GMT ratios); within-group CIs were not calculated. OPA for serotype 3 contained in Prevnar 13™ and V114 was determined using a MOPA. The analysis population included all randomized participants without protocol deviations, such as failure to receive study vaccine or receipt of prohibited medication prior to study vaccination.

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	598	598		
Units: Titers				
number (not applicable)	216.2	135.1		

Statistical analyses

Statistical analysis title	Serotype 3 (Shared)
Comparison groups	V114 v Prevnar 13™
Number of subjects included in analysis	1196
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	cLDA
Parameter estimate	GMT Ratio
Point estimate	1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.38
upper limit	1.85

Secondary: Percentage of Participants with ≥4-Fold Rise in Serotype-specific OPA for Serotype 3 OPA Responses

End point title	Percentage of Participants with ≥4-Fold Rise in Serotype-specific OPA for Serotype 3 OPA Responses

End point description:

Activity for serotype 3 contained in Prevnar 13™ and V114 was determined using a MOPA. The observed response percentage of participants (m/n) who had ≥4-fold rise in OPA titers were calculated from baseline to postvaccination. n=Number of participants contributing to the analysis; m=Number of participants with the indicated response. Per the statistical analysis plan, the only CIs calculated were the between-group CIs (for the percentage point difference); within-group CIs were not calculated.

End point type	Secondary

End point timeframe:

Day 1 (Baseline) and Day 30

End point values	V114	Prevnar 13™		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	580	576		
Units: Percentage of Participants				
number (not applicable)	70.2	58.7		

Statistical analyses

Statistical analysis title	Serotype 3 (Shared) ≥4-Fold Rise in OPA
Comparison groups	V114 v Prevnar 13™
Number of subjects included in analysis	1156
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Miettinen & Nurminen
Parameter estimate	Percentage Point Difference
Point estimate	11.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	6
upper limit	16.9

Secondary: Geometric Mean Concentration of Serotype-specific IgG at Day 30

End point title	Geometric Mean Concentration of Serotype-specific IgG at Day 30

End point description:

Serotype-specific Immunoglobulin G (IgG) geometric mean concentrations (GMCs) (estimated) and GMC ratios with 95% confidence intervals (CIs) were calculated using a cLDA model utilizing data from both vaccination groups. Per the statistical analysis plan, the only CIs calculated were the between-group CIs (for the GMC ratios); within-group CIs were not calculated. IgG for the serotypes contained in Prevnar 13™ and V114 (13 serotypes shared with Prevnar 13™ and 2 serotypes unique to V114) will be

determined using an electrochemiluminescence assay. The analysis population included all randomized participants without protocol deviations, such as failure to receive study vaccine or receipt of prohibited medication prior to study vaccination.

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	602	600		
Units: µg/mL				
number (not applicable)				
Serotype 1 (Shared) (n=598, 598)	5.30	7.34		
Serotype 3 (Shared) (n=598, 598)	0.96	0.64		
Serotype 4 (Shared) (n=598, 598)	1.88	2.62		
Serotype 5 (Shared) (n=598, 598)	4.57	5.56		
Serotype 6A (Shared) (n=598, 598)	7.21	7.01		
Serotype 6B (Shared) (n=598, 598)	8.60	6.19		
Serotype 7F (Shared) (n=598, 598)	6.18	8.09		
Serotype 9V (Shared) (n=598, 598)	4.77	5.52		
Serotype 14 (Shared) (n=598, 598)	9.39	12.30		
Serotype 18C (Shared) (n=598, 598)	8.99	10.00		
Serotype 19A (Shared) (n=598, 598)	14.60	17.38		
Serotype 19F (Shared) (n=598, 598)	8.77	9.70		
Serotype 23F (Shared) (n=598, 598)	6.67	6.13		
Serotype 22F (Unique to V114) (n=598, 598)	3.44	0.32		
Serotype 33F (Unique to V114) (n=598, 598)	11.05	1.23		

Statistical analyses

Statistical analysis title	Serotype 1 (Shared)
Comparison groups	V114 v Prevnar 13™
Number of subjects included in analysis	1202
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	GMC Ratio
Point estimate	0.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.62
upper limit	0.83

Statistical analysis title	Serotype 3 (Shared)
Comparison groups	V114 v Prevnar 13™
Number of subjects included in analysis	1202
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	GMC Ratio
Point estimate	1.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.33
upper limit	1.71

Statistical analysis title	Serotype 4 (Shared)
Comparison groups	V114 v Prevnar 13™
Number of subjects included in analysis	1202
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	GMC Ratio
Point estimate	0.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.62
upper limit	0.83

Statistical analysis title	Serotype 5 (Shared)
Comparison groups	V114 v Prevnar 13™
Number of subjects included in analysis	1202
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	GMC Ratio
Point estimate	0.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	0.96

Statistical analysis title	Serotype 6A (Shared)
Comparison groups	V114 v Prevnar 13™

Number of subjects included in analysis	1202
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	GMC Ratio
Point estimate	1.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.87
upper limit	1.21

Statistical analysis title	Serotype 6B (Shared)
Comparison groups	V114 v Prevnar 13™
Number of subjects included in analysis	1202
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	GMC Ratio
Point estimate	1.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.17
upper limit	1.64

Statistical analysis title	Serotype 7F (Shared)
Comparison groups	V114 v Prevnar 13™
Number of subjects included in analysis	1202
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	GMC Ratio
Point estimate	0.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.66
upper limit	0.89

Statistical analysis title	Serotype 9V (Shared)
Comparison groups	V114 v Prevnar 13™

Number of subjects included in analysis	1202
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	GMC Ratio
Point estimate	0.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.75
upper limit	1

Statistical analysis title	Serotype 14 (Shared)
Comparison groups	V114 v Prevnar 13™
Number of subjects included in analysis	1202
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	GMC Ratio
Point estimate	0.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.65
upper limit	0.89

Statistical analysis title	Serotype 18C (Shared)
Comparison groups	V114 v Prevnar 13™
Number of subjects included in analysis	1202
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	GMC Ratio
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.77
upper limit	1.05

Statistical analysis title	Serotype 19A (Shared)
Comparison groups	V114 v Prevnar 13™

Number of subjects included in analysis	1202
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	GMC Ratio
Point estimate	0.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.73
upper limit	0.97

Statistical analysis title	Serotype 19F (Shared)
Comparison groups	V114 v Prevnar 13™
Number of subjects included in analysis	1202
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	GMC Ratio
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.78
upper limit	1.05

Statistical analysis title	Serotype 23F (Shared)
Comparison groups	V114 v Prevnar 13™
Number of subjects included in analysis	1202
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	GMC Ratio
Point estimate	1.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.92
upper limit	1.28

Statistical analysis title	Serotype 22F (Unique to V114)
Comparison groups	V114 v Prevnar 13™

Number of subjects included in analysis	1202
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	GMC Ratio
Point estimate	10.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	9.37
upper limit	12.03

Statistical analysis title	Serotype 33F (Unique to V114)
Comparison groups	V114 v Prevnar 13™
Number of subjects included in analysis	1202
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	GMC Ratio
Point estimate	8.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	8
upper limit	10.07

Secondary: Geometric Mean Fold Rise in Serotype-specific OPA

End point title	Geometric Mean Fold Rise in Serotype-specific OPA

End point description:

Activity for the serotypes contained in Prevnar 13™ and V114 (13 serotypes shared with Prevnar 13™ and 2 serotypes unique to V114) was determined using a Multiplexed Opsonophagocytic 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 analysis population included all randomized participants without protocol deviations, such as failure to receive study vaccine or receipt of prohibited medication prior to study vaccination.

End point type	Secondary

End point timeframe:

Day 1 (Baseline) and Day 30

End point values	V114	Prevnar 13™		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	602	600		
Units: Ratio				
geometric mean (confidence interval 95%)				
Serotype 1 (Shared) (n=583, 573)	14.3 (12.5 to 16.4)	18.7 (16.2 to 21.5)		

Serotype 3 (Shared) (n=580, 576)	7.7 (7.0 to 8.6)	5.2 (4.7 to 5.7)		
Serotype 4 (Shared) (n=586, 578)	17.8 (15.7 to 20.3)	24.4 (21.3 to 27.8)		
Serotype 5 (Shared) (n=588, 584)	12.3 (10.7 to 14.2)	15.3 (13.2 to 17.6)		
Serotype 6A (Shared) (n=545, 550)	13.0 (11.4 to 14.9)	13.3 (11.6 to 15.2)		
Serotype 6B (Shared) (n=579, 576)	26.3 (22.4 to 30.8)	21.6 (18.5 to 25.2)		
Serotype 7F (Shared) (n=566, 555)	12.0 (10.3 to 13.9)	14.1 (12.1 to 16.5)		
Serotype 9V (Shared) (n=578, 573)	5.3 (4.8 to 6.0)	6.3 (5.6 to 7.1)		
Serotype 14 (Shared) (n=579,576)	6.2 (5.4 to 7.2)	8.7 (7.5 to 10.0)		
Serotype 18C (Shared) (n=578,579)	11.3 (10.0 to 12.9)	10.4 (9.1 to 11.8)		
Serotype 19A (Shared) (n=581,575)	10.9 (9.5 to 12.5)	13.1 (11.4 to 15.1)		
Serotype 19F (Shared) (n=579,576)	6.6 (5.9 to 7.5)	7.4 (6.6 to 8.3)		
Serotype 23F (Shared) (n=555,555)	16.2 (14.0 to 18.9)	13.5 (11.5 to 15.9)		
Serotype 22F (Unique to V114) (n=524,498)	28.3 (22.8 to 35.1)	1.2 (1.0 to 1.4)		
Serotype 33F (Unique to V114)(n=578,560)	7.4 (6.4 to 8.6)	1.0 (1.0 to 1.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Fold Rise in Serotype-specific IgG

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

End point description:

Activity for the serotypes contained in Prevnar 13™ and V114 (13 serotypes shared with Prevnar 13™ and 2 serotypes unique to V114) was determined using an electrochemiluminescence 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 analysis population included all randomized participants without protocol deviations, such as failure to receive study vaccine or receipt of prohibited medication prior to study vaccination.

End point type	Secondary

End point timeframe:

Day 1 (Baseline) and Day 30

End point values	V114	Prevnar 13™		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	602	600		
Units: Ratio				
geometric mean (confidence interval 95%)				
Serotype 1 (Shared) (n=588,584)	10.6 (9.4 to 12.0)	14.7 (13.1 to 16.6)		
Serotype 3 (Shared) (n=588,582)	6.8 (6.2 to 7.6)	4.7 (4.2 to 5.1)		

Serotype 4 (Shared) (n=586,583)	8.0 (7.2 to 9.0)	11.2 (10.0 to 12.5)		
Serotype 5 (Shared) (n=588,584)	4.7 (4.2 to 5.2)	5.8 (5.2 to 6.5)		
Serotype 6A (Shared) (n=588,584)	19.9 (17.6 to 22.6)	19.7 (17.4 to 22.3)		
Serotype 6B (Shared) (n=588,582)	19.1 (16.8 to 21.7)	13.8 (12.3 to 15.6)		
Serotype 7F (Shared) (n=588,584)	12.3 (10.9 to 13.9)	15.8 (13.9 to 18.0)		
Serotype 9V (Shared) (n=588,584)	9.9 (8.9 to 11.1)	11.1 (9.9 to 12.4)		
Serotype 14 (Shared) (n=587,583)	5.1 (4.5 to 5.7)	7.2 (6.3 to 8.2)		
Serotype 18C (Shared) (n=588,583)	12.8 (11.3 to 14.5)	14.3 (12.6 to 16.2)		
Serotype 19A (Shared) (n=588,584)	8.7 (7.8 to 9.8)	10.6 (9.5 to 11.9)		
Serotype 19F (Shared) (n=583,580)	10.9 (9.7 to 12.3)	12.5 (11.1 to 14.0)		
Serotype 23F (Shared) (n=586,584)	13.5 (11.9 to 15.3)	12.2 (10.8 to 13.7)		
Serotype 22F (Unique to V114) (n=588,583)	11.7 (10.3 to 13.3)	1.1 (1.1 to 1.1)		
Serotype 33F (Unique to V114) (n=588,584)	9.1 (8.0 to 10.2)	1.0 (1.0 to 1.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With ≥4-Fold Rise in Serotype-specific OPA Titer

End point title	Percentage of Participants With ≥4-Fold Rise in Serotype-specific OPA Titer

End point description:

Activity for the serotypes contained in Prevnar 13™ and V114 (13 serotypes shared with Prevnar 13™ and 2 serotypes unique to V114) was determined using a multiplexed opsonophagocytic assay. The percentage of participants who had ≥4-fold rise in OPA titers were calculated from baseline to postvaccination. The analysis population included all randomized participants without protocol deviations, such as failure to receive study vaccine or receipt of prohibited medication prior to study vaccination.

End point type	Secondary

End point timeframe:

Day 1 (Baseline) and Day 30

End point values	V114	Prevnar 13™		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	602	600		
Units: Percentage of Participants				
number (confidence interval 95%)				
Serotype 1 (Shared) (n=583,573)	75.1 (71.4 to 78.6)	77.7 (74.0 to 81.0)		

Serotype 3 (Shared) (n=580,576)	70.2 (66.3 to 73.9)	58.7 (54.5 to 62.7)		
Serotype 4 (Shared) (n=586,578)	79.5 (76.0 to 82.7)	84.8 (81.6 to 87.6)		
Serotype 5 (Shared) (n=588,584)	71.6 (67.8 to 75.2)	75.3 (71.6 to 78.8)		
Serotype 6A (Shared) (n=545,550)	76.5 (72.7 to 80.0)	74.9 (71.1 to 78.5)		
Serotype 6B (Shared) (n=579,576)	81.2 (77.7 to 84.3)	79.2 (75.6 to 82.4)		
Serotype 7F (Shared) (n=566,555)	66.4 (62.4 to 70.3)	72.4 (68.5 to 76.1)		
Serotype 9V (Shared) (n=578,573)	54.0 (49.8 to 58.1)	60.0 (55.9 to 64.1)		
Serotype 14 (Shared) (n=579,576)	52.2 (48.0 to 56.3)	60.8 (56.6 to 64.8)		
Serotype 18C (Shared) (n=578,579)	71.3 (67.4 to 74.9)	69.1 (65.1 to 72.8)		
Serotype 19A (Shared) (n=581,575)	70.6 (66.7 to 74.2)	71.1 (67.2 to 74.8)		
Serotype 19F (Shared) (n=579,576)	62.0 (57.9 to 66.0)	65.1 (61.1 to 69.0)		
Serotype 23F (Shared) (n=555,555)	75.0 (71.1 to 78.5)	71.4 (67.4 to 75.1)		
Serotype 22F (Unique to V114) (n=524,498)	71.4 (67.3 to 75.2)	14.3 (11.3 to 17.6)		
Serotype 33F (Unique to V114) (n=578,560)	56.7 (52.6 to 60.8)	6.3 (4.4 to 8.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with ≥4-Fold Rise in Serotype-specific IgG Concentration

End point title	Percentage of Participants with ≥4-Fold Rise in Serotype-specific IgG Concentration

End point description:

Activity for the serotypes contained in Prevnar 13™ and V114 (13 serotypes shared with Prevnar 13™ and 2 serotypes unique to V114) will be determined using an electrochemiluminescence assay. The percentage of participants who had ≥4-fold rise in IgG concentration are calculated from baseline to postvaccination. The analysis population included all randomized participants without protocol deviations, such as failure to receive study vaccine or receipt of prohibited medication prior to study vaccination.

End point type	Secondary

End point timeframe:

Day 1 (Baseline) and Day 30

End point values	V114	Prevnar 13™		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	602	600		
Units: Percentage of Participants				
number (confidence interval 95%)				
Serotype 1 (Shared) (n=588,584)	73.1 (69.4 to 76.7)	78.4 (74.9 to 81.7)		
Serotype 3 (Shared) (n=588,582)	61.6 (57.5 to 65.5)	51.4 (47.2 to 55.5)		
Serotype 4 (Shared) (n=586,583)	65.0 (61.0 to 68.9)	76.0 (72.3 to 79.4)		
Serotype 5 (Shared) (n=588,584)	45.1 (41.0 to 49.2)	53.4 (49.3 to 57.5)		
Serotype 6A (Shared) (n=588,584)	83.5 (80.3 to 86.4)	83.4 (80.1 to 86.3)		
Serotype 6B (Shared) (n=588,582)	82.8 (79.5 to 85.8)	77.5 (73.9 to 80.8)		
Serotype 7F (Shared) (n=588,584)	73.5 (69.7 to 77.0)	78.6 (75.0 to 81.9)		
Serotype 9V (Shared) (n=588,584)	69.6 (65.7 to 73.3)	75.5 (71.8 to 79.0)		
Serotype 14 (Shared) (n=587,583)	49.4 (45.3 to 53.5)	59.5 (55.4 to 63.5)		
Serotype 18C (Shared) (n=588,583)	73.1 (69.4 to 76.7)	76.3 (72.7 to 79.7)		
Serotype 19A (Shared) (n=588,584)	67.2 (63.2 to 71.0)	71.2 (67.4 to 74.9)		
Serotype 19F (Shared) (n=583,580)	69.5 (65.6 to 73.2)	75.5 (71.8 to 79.0)		
Serotype 23F (Shared) (n=586,584)	74.9 (71.2 to 78.4)	74.3 (70.6 to 77.8)		
Serotype 22F (Unique to V114) (n=588,583)	71.4 (67.6 to 75.0)	1.7 (0.8 to 3.1)		
Serotype 33F (Unique to V114) (n=588,584)	66.5 (62.5 to 70.3)	1.7 (0.8 to 3.1)		

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 vaccination; Serious adverse events and all-cause mortality: Up to ~Month 6 (Up to 194 days after vaccination).

Adverse event reporting additional description:

The analysis population for adverse events and serious adverse events: all randomized participants who received study vaccination and were included in the intervention group according to the intervention they received. All randomized participants were included in the number of deaths (all causes).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	V114

Reporting group description: -

Reporting group title	PCV13

Reporting group description: -

Serious adverse events	V114	PCV13	
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 602 (1.50%)	13 / 600 (2.17%)	
number of deaths (all causes)	1	1	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 602 (0.00%)	1 / 600 (0.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal carcinoma			
subjects affected / exposed	0 / 602 (0.00%)	1 / 600 (0.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung neoplasm malignant			
subjects affected / exposed	0 / 602 (0.00%)	1 / 600 (0.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-small cell lung cancer			

subjects affected / exposed	1 / 602 (0.17%)	0 / 600 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer			
subjects affected / exposed	0 / 602 (0.00%)	1 / 600 (0.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer stage II			
subjects affected / exposed	0 / 602 (0.00%)	1 / 600 (0.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Meniscus injury			
subjects affected / exposed	1 / 602 (0.17%)	0 / 600 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 602 (0.00%)	1 / 600 (0.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina unstable			
subjects affected / exposed	0 / 602 (0.00%)	1 / 600 (0.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arrhythmia			
subjects affected / exposed	0 / 602 (0.00%)	1 / 600 (0.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Atrial fibrillation			
subjects affected / exposed	1 / 602 (0.17%)	0 / 600 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Myocardial infarction			
subjects affected / exposed	1 / 602 (0.17%)	0 / 600 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 602 (0.00%)	1 / 600 (0.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Death			
subjects affected / exposed	1 / 602 (0.17%)	0 / 600 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Gastrointestinal disorders			
Incarcerated umbilical hernia			
subjects affected / exposed	1 / 602 (0.17%)	0 / 600 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophagitis ulcerative			
subjects affected / exposed	0 / 602 (0.00%)	1 / 600 (0.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Pelvic pain			
subjects affected / exposed	0 / 602 (0.00%)	1 / 600 (0.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 602 (0.00%)	1 / 600 (0.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			

Ureterolithiasis			
subjects affected / exposed	0 / 602 (0.00%)	1 / 600 (0.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 602 (0.17%)	0 / 600 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	1 / 602 (0.17%)	0 / 600 (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			
Diverticulitis			
subjects affected / exposed	1 / 602 (0.17%)	0 / 600 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			
subjects affected / exposed	0 / 602 (0.00%)	1 / 600 (0.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	V114	PCV13	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	395 / 602 (65.61%)	336 / 600 (56.00%)	
Nervous system disorders			
Headache			
subjects affected / exposed	70 / 602 (11.63%)	78 / 600 (13.00%)	
occurrences (all)	93	105	
General disorders and administration site conditions			

Fatigue			
subjects affected / exposed	105 / 602 (17.44%)	104 / 600 (17.33%)	
occurrences (all)	144	140	
Injection site erythema			
subjects affected / exposed	60 / 602 (9.97%)	73 / 600 (12.17%)	
occurrences (all)	62	77	
Injection site pain			
subjects affected / exposed	327 / 602 (54.32%)	257 / 600 (42.83%)	
occurrences (all)	367	294	
Injection site swelling			
subjects affected / exposed	76 / 602 (12.62%)	73 / 600 (12.17%)	
occurrences (all)	79	78	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	32 / 602 (5.32%)	33 / 600 (5.50%)	
occurrences (all)	38	39	
Myalgia			
subjects affected / exposed	93 / 602 (15.45%)	72 / 600 (12.00%)	
occurrences (all)	111	85	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 April 2020	Amendment 01- Revisions were made to include assessment of superiority for Serotype 3 and to include a revised statistical criterion for assessment of superiority for serotypes 22F and 33F. to make it a more stringent test.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported