# 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 Japanese Infants

## Summary

| | |
|---|---|
| EudraCT number | 2019-003644-68 |
| Trial protocol | Outside EU/EEA |
| Global end of trial date | 09 February 2022 |

### Results information

| | |
|---|---|
| Result version number | v3 (current) |
| This version publication date | 25 December 2022 |
| First version publication date | 24 July 2022 |
| Version creation reason | |

## Trial information

### Trial identification

| | |
|---|---|
| Sponsor protocol code | V114-033 |

### Additional study identifiers

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT04384107 |
| WHO universal trial number (UTN) | - |
| Other trial identifiers | JAPIC-CTI: 205287 |

Notes:

### Sponsors

| | |
|---|---|
| Sponsor organisation name | Merck Sharp & Dohme LLC |
| Sponsor organisation address | 126 East Lincoln Avenue, P.O. Box 2000, Rahway, NJ, 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? | Yes |

Notes:

## Results analysis stage

| | |
|---|---|
| Analysis stage | Final |
| Date of interim/final analysis | 01 December 2021 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 01 December 2021 |
| Global end of trial reached? | Yes |
| Global end of trial date | 09 February 2022 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

The purpose of this clinical study is to evaluate the safety and immunogenicity of a 4-dose schedule (3-dose primary series followed by a toddler dose) of V114 compared with Pneumococcal 13-valent Conjugate Vaccine (PCV13). The hypotheses are that: 1) V114 is non-inferior to PCV13 for the 13 shared serotypes between V114 and PCV13 based on the response rates at 30 days following dose 3; 2) V114 is non-inferior to PCV13 for the 2 unique V114 serotypes based on the response rate of the 2 unique V114 serotypes at 30 days following dose 3; 3) V114 is non-inferior to PCV13 for the 13 shared serotypes between V114 and PCV13 based on anti-pneumococcal polysaccharide (PnPs) serotype-specific Immunoglobulin G (IgG) geometric mean concentrations (GMCs) at 30 days following dose 3.

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 | 01 July 2020 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Japan: 694 |
| Worldwide total number of subjects | 694 |
| EEA total number of subjects | 0 |

Notes:

### Subjects enrolled per age group

| | |
|---|---|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 694 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |

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

## Subject disposition

### Recruitment

Recruitment details:

This study enrolled healthy Japanese infants at 2 to 6 months of age.

### Pre-assignment

Screening details:

694 infants were randomized in a 1:1 ratio with stratification into 3 categories by age category (2 months, 3 months and 4 to 6 months of age), to receive either V114 or PCV13.

### Period 1

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

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | V114 |

Arm description:

Participants received single 0.5 mL subcutaneous injection of V114 administered at 2 to 6 months of age, and second and third dose is administered at an interval of ≥27 days from the prior dose. The fourth dose is administered at 12 to 15 months of age.

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

Dosage and administration details:

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

| | |
|---|---|
| **Arm title** | PCV13 |

Arm description:

Participants received a single 0.5 mL subcutaneous injection of PCV13 administered at 2 to 6 months of age, and second and third dose is administered at an interval of ≥27 days from the prior dose. The fourth dose is administered at 12 to 15 months of age.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | PCV13 |
| Investigational medicinal product code | |
| Other name | Prevnar 13™ |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

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

| **Number of subjects in period 1** | V114 | PCV13 |
|---|---|---|
| Started | 347 | 347 |
| Dose 1 | 347 | 346 |
| Dose 2 | 344 | 346 |
| Dose 3 | 343 | 346 |
| Dose 4 | 340 | 342 |
| Completed | 338 | 341 |
| Not completed | 9 | 6 |
| Withdrawal By Parent/Guardian | 8 | 6 |
| Lost to follow-up | 1 | - |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | V114 |
| Reporting group description: | |
| Participants received single 0.5 mL subcutaneous injection of V114 administered at 2 to 6 months of age, and second and third dose is administered at an interval of ≥27 days from the prior dose. The fourth dose is administered at 12 to 15 months of age. | |
| Reporting group title | PCV13 |
| Reporting group description: | |
| Participants received a single 0.5 mL subcutaneous injection of PCV13 administered at 2 to 6 months of age, and second and third dose is administered at an interval of ≥27 days from the prior dose. The fourth dose is administered at 12 to 15 months of age. | |

| Reporting group values | V114 | PCV13 | Total |
|---|---|---|---|
| Number of subjects | 347 | 347 | 694 |
| Age Categorical<br>Units: Subjects | | | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 347 | 347 | 694 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 0 | 0 | 0 |
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |
| Age Continuous<br>Units: months | | | |
| arithmetic mean | 2.4 | 2.4 | |
| standard deviation | ± 0.4 | ± 0.4 | - |
| Gender Categorical<br>Units: Subjects | | | |
| Female | 166 | 173 | 339 |
| Male | 181 | 174 | 355 |
| Race<br>Units: Subjects | | | |
| Asian | 347 | 347 | 694 |
| Ethnicity<br>Units: Subjects | | | |
| Not Hispanic or Latino | 347 | 347 | 694 |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | V114 |
| Reporting group description: | |
| Participants received single 0.5 mL subcutaneous injection of V114 administered at 2 to 6 months of age, and second and third dose is administered at an interval of ≥27 days from the prior dose. The fourth dose is administered at 12 to 15 months of age. | |
| Reporting group title | PCV13 |
| Reporting group description: | |
| Participants received a single 0.5 mL subcutaneous injection of PCV13 administered at 2 to 6 months of age, and second and third dose is administered at an interval of ≥27 days from the prior dose. The fourth dose is administered at 12 to 15 months of age. | |

### Primary: Percentage of Participants with Solicited Injection-Site Adverse Events

| | |
|---|---|
| End point title | Percentage of Participants with Solicited Injection-Site Adverse Events |
| End point description: | |
| An adverse event (AE) is any untoward medical occurrence in a patient or clinical study participant, temporally associated with the use of study treatment, whether or not considered related to the study treatment. Following any injection with either V114 or PCV13 the percentage of participants with solicited injection-site AEs was assessed. The solicited injection-site AEs were erythema, induration, pain, and swelling. All randomized participants who received at least 1 dose of study vaccination were analyzed. One participant in the PCV13 group did not receive PCV13 and therefore was not included in the analysis for this end point. | |
| End point type | Primary |
| End point timeframe: | |
| Day 1 to Day 14 post any vaccination, up to a total of 13.5 months | |

| End point values | V114 | PCV13 | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 347 | 346 | | |
| Units: Percentage of Participants | | | | |
| number (not applicable) | | | | |
| Injection site erythema | 88.2 | 89.3 | | |
| Injection site induration | 81.0 | 81.2 | | |
| Injection site pain | 31.1 | 24.0 | | |
| Injection site swelling | 75.8 | 79.8 | | |

### Statistical analyses

| | |
|---|---|
| **Statistical analysis title** | Injection site erythema |
| Comparison groups | V114 v PCV13 |

| | |
|---|---|
| Number of subjects included in analysis | 693 |
| Analysis specification | Pre-specified |
| Analysis type | other[1] |
| P-value | = 0.641 |
| Method | Miettinen & Nurminen |
| Parameter estimate | Difference in Percent |
| Point estimate | -1.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -5.9 |
| upper limit | 3.6 |

Notes:

[1] - Estimated differences, confidence intervals (CIs), and p-values are calculated based on the Miettinen & Nurminen method and are provided in accordance with the statistical analysis plan.

| **Statistical analysis title** | Injection site induration |
|---|---|
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 693 |
| Analysis specification | Pre-specified |
| Analysis type | other[2] |
| P-value | = 0.937 |
| Method | Miettinen & Nurminen |
| Parameter estimate | Difference in Percent |
| Point estimate | -0.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -6.1 |
| upper limit | 5.6 |

Notes:

[2] - Estimated differences, confidence intervals (CIs), and p-values are calculated based on the Miettinen & Nurminen method and are provided in accordance with the statistical analysis plan.

| **Statistical analysis title** | Injection site pain |
|---|---|
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 693 |
| Analysis specification | Pre-specified |
| Analysis type | other[3] |
| P-value | = 0.036 |
| Method | Miettinen & Nurminen |
| Parameter estimate | Difference in Percent |
| Point estimate | 7.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.5 |
| upper limit | 13.8 |

Notes:

[3] - Estimated differences, confidence intervals (CIs), and p-values are calculated based on the Miettinen & Nurminen method and are provided in accordance with the statistical analysis plan.

| **Statistical analysis title** | Injection site swelling |
|---|---|

| | |
|---|---|
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 693 |
| Analysis specification | Pre-specified |
| Analysis type | other[4] |
| P-value | = 0.208 |
| Method | Miettinen & Nurminen |
| Parameter estimate | Difference in Percent |
| Point estimate | -4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -10.2 |
| upper limit | 2.2 |

Notes:

[4] - Estimated differences, confidence intervals (CIs), and p-values are calculated based on the Miettinen & Nurminen method and are provided in accordance with the statistical analysis plan.

## 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 any of the injections with either V114 or PCV13, the percentage of participants with solicited systemic AEs was assessed. The solicited systemic AEs assessed were decreased appetite, irritability, somnolence, and urticaria. All randomized participants who received at least 1 dose of study vaccination were analyzed. One participant in the PCV13 group did not receive PCV13 and therefore was not included in the analysis for this end point.

| | |
|---|---|
| End point type | Primary |

End point timeframe:

Day 1 to Day 14 post any vaccination, up to a total of 13.5 months

| **End point values** | V114 | PCV13 | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 347 | 346 | | |
| Units: Percentage of Participants | | | | |
| number (not applicable) | | | | |
| Decreased appetite | 23.9 | 24.3 | | |
| Irritability | 66.6 | 60.7 | | |
| Somnolence | 55.9 | 54.9 | | |
| Urticaria | 4.0 | 4.3 | | |

## Statistical analyses

| **Statistical analysis title** | Decreased appetite |
|---|---|
| Comparison groups | V114 v PCV13 |

| | |
|---|---|
| Number of subjects included in analysis | 693 |
| Analysis specification | Pre-specified |
| Analysis type | other[5] |
| P-value | = 0.912 |
| Method | Miettinen & Nurminen |
| Parameter estimate | Difference in Percent |
| Point estimate | -0.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -6.7 |
| upper limit | 6 |

Notes:

[5] - Estimated differences, confidence intervals (CIs), and p-values are calculated based on the Miettinen & Nurminen method and are provided in accordance with the statistical analysis plan.

| **Statistical analysis title** | Irritability |
|---|---|
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 693 |
| Analysis specification | Pre-specified |
| Analysis type | other[6] |
| P-value | = 0.108 |
| Method | Miettinen & Nurminen |
| Parameter estimate | Difference in Percent |
| Point estimate | 5.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.3 |
| upper limit | 13 |

Notes:

[6] - Estimated differences, confidence intervals (CIs), and p-values are calculated based on the Miettinen & Nurminen method and are provided in accordance with the statistical analysis plan.

| **Statistical analysis title** | Somnolence |
|---|---|
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 693 |
| Analysis specification | Pre-specified |
| Analysis type | other[7] |
| P-value | = 0.792 |
| Method | Miettinen & Nurminen |
| Parameter estimate | Difference in Percent |
| Point estimate | 1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -6.4 |
| upper limit | 8.4 |

Notes:

[7] - Estimated differences, confidence intervals (CIs), and p-values are calculated based on the Miettinen & Nurminen method and are provided in accordance with the statistical analysis plan.

| **Statistical analysis title** | Urticaria |
|---|---|

| | |
|---|---|
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 693 |
| Analysis specification | Pre-specified |
| Analysis type | other[8] |
| P-value | = 0.843 |
| Method | Miettinen & Nurminen |
| Parameter estimate | Difference in Percent |
| Point estimate | -0.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.5 |
| upper limit | 2.8 |

Notes:

[8] - Estimated differences, confidence intervals (CIs), and p-values are calculated based on the Miettinen & Nurminen method and are provided in accordance with the statistical analysis plan.

## Primary: Percentage of Participants with Vaccine-Related Serious Adverse Events

| | |
|---|---|
| End point title | Percentage of Participants with Vaccine-Related Serious Adverse Events |

End point description:

A serious adverse event (SAE) is an AE that is life-threatening, requires or prolongs an existing hospitalization, results in persistent or significant disability or incapacity, is a congenital anomaly or birth defect, or is another important medical event deemed such by medical or scientific judgment. The percentage of participants with a vaccine-related SAE following dose 1 (with either V114 or PCV13) was reported. Vaccine-related SAEs were counted starting after vaccine dose 1 through completion of study. All randomized participants who received at least 1 dose of the relevant study vaccination for the timepoint of interest were analyzed. One participant in the PCV13 group did not receive PCV13 and therefore was not included in the analysis for this end point.

| | |
|---|---|
| End point type | Primary |

End point timeframe:

~1 month after Dose 4 (Up to 14 months)

| **End point values** | V114 | PCV13 | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 347 | 346 | | |
| Units: Percentage of Participants | | | | |
| number (not applicable) | 0.3 | 0.3 | | |

## Statistical analyses

| **Statistical analysis title** | Vaccine-related SAEs |
|---|---|

Statistical analysis description:

Estimated differences and CIs are calculated based on the Miettinen & Nurminen method and are provided in accordance with the statistical analysis plan.

| | |
|---|---|
| Comparison groups | V114 v PCV13 |

| | |
|---|---|
| Number of subjects included in analysis | 693 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Method | Miettinen & Nurminen |
| Parameter estimate | Difference in Percent |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.4 |
| upper limit | 1.3 |

## Primary: Percentage of Participants Meeting the Serotype Specific Immunoglobulin G Threshold Value of ≥0.35 µg/mL for Each Serotype in V114 After Dose 3

| | |
|---|---|
| End point title | Percentage of Participants Meeting the Serotype Specific Immunoglobulin G Threshold Value of ≥0.35 µg/mL for Each Serotype in V114 After Dose 3 |

End point description:

The anti-pneumococcal polysaccharide (PnPs) serotype-specific immunoglobulin G (IgG) response rates (percentage of participants meeting serotype-specific IgG threshold value of ≥0.35 µg/mL for participants administered V114 versus participants administered PCV13) for the 15 serotypes contained in V114 were determined using an electrochemiluminescence assay. All randomized participants without protocol deviations that could have substantially impacted the results of the immunogenicity endpoint and who had sufficient data to perform the analyses were analyzed. One participant in the PCV13 group did not receive PCV13 and therefore was not included in the analysis for this end point. A value of '9999' indicates that data could not be calculated, as the analysis represents the difference between response rate to each serotype in recipients of V114 and lowest response (Serotype 3 at 97.7) in recipients of PCV13 for shared serotypes.

| | |
|---|---|
| End point type | Primary |

End point timeframe:

30 Days after Dose 3, up to a total of 11 months

| **End point values** | V114 | PCV13 | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 339 | 343 | | |
| Units: Percentage of Participants | | | | |
| number (not applicable) | | | | |
| Serotype 1 (Shared) (n=339, 343) | 99.7 | 100.0 | | |
| Serotype 3 (Shared) (n=339, 343) | 100.0 | 97.7 | | |
| Serotype 4 (Shared) (n=339, 343) | 100.0 | 100.0 | | |
| Serotype 5 (Shared) (n=338, 343) | 98.8 | 100.0 | | |
| Serotype 6A (Shared) (n=339, 343) | 99.1 | 100.0 | | |
| Serotype 6B (Shared) (n=339, 343) | 95.0 | 98.8 | | |
| Serotype 7F (Shared) (n=339, 343) | 99.7 | 100.0 | | |
| Serotype 9V (Shared) (n=339, 343) | 99.7 | 100.0 | | |
| Serotype 14 (Shared) (n=339, 342) | 99.4 | 99.7 | | |
| Serotype 18C (Shared) (n=339, 343) | 98.8 | 100.0 | | |
| Serotype 19A (Shared) (n=339, 343) | 99.7 | 100.0 | | |
| Serotype 19F (Shared) (n=339, 343) | 100.0 | 100.0 | | |

| | | | | |
|---|---|---|---|---|
| Serotype 23F (Shared) (n=338, 342) | 97.9 | 99.7 | | |
| Serotype 22F (Unique to V114) (n=339, 343) | 99.7 | 9999 | | |
| Serotype 33F (Unique to V114) (n=339, 343) | 90.9 | 9999 | | |

## Statistical analyses

| **Statistical analysis title** | Serotype 1 |
|---|---|
| Statistical analysis description: Participants With IgG ≥0.35 µg/mL | |
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 682 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority[9] |
| P-value | < 0.001 |
| Method | Miettinen and Nurminen |
| Parameter estimate | Difference in Percent |
| Point estimate | -0.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.7 |
| upper limit | 0.8 |

Notes:

[9] - The stratum-adjusted proportion difference using the Cochran-Mantel-Haenszel weight, and the corresponding 95% CI and p-value based on the method of Miettinen and Nurminen stratified by age category (2 months of age, ≥3 months of age). A conclusion of non-inferiority of V114 to PCV13 is based on the lower bound of the 2-sided 95% CI for the difference in percentages (V114 - PCV13) being >-10 percentage points (1-sided p-value <0.025).

| **Statistical analysis title** | Serotype 3 |
|---|---|
| Statistical analysis description: Participants With IgG ≥0.35 µg/mL | |
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 682 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority[10] |
| P-value | < 0.001 |
| Method | Miettinen and Nurminen |
| Parameter estimate | Difference in Percent |
| Point estimate | 2.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1 |
| upper limit | 4.5 |

Notes:

[10] - The stratum-adjusted proportion difference using the Cochran-Mantel-Haenszel weight, and the corresponding 95% CI and p-value based on the method of Miettinen and Nurminen stratified by age category (2 months of age, ≥3 months of age). A conclusion of non-inferiority of V114 to PCV13 is based on the lower bound of the 2-sided 95% CI for the difference in percentages (V114 - PCV13) being >-10 percentage points (1-sided p-value <0.025).

| **Statistical analysis title** | Serotype 4 |
|---|---|
| Statistical analysis description: | |
| Participants With IgG ≥0.35 µg/mL | |
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 682 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority[11] |
| P-value | < 0.001 |
| Method | Miettinen and Nurminen |
| Parameter estimate | Difference in Percent |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.1 |
| upper limit | 1.1 |

Notes:

[11] - The stratum-adjusted proportion difference using the Cochran-Mantel-Haenszel weight, and the corresponding 95% CI and p-value based on the method of Miettinen and Nurminen stratified by age category (2 months of age, ≥3 months of age). A conclusion of non-inferiority of V114 to PCV13 is based on the lower bound of the 2-sided 95% CI for the difference in percentages (V114 - PCV13) being >-10 percentage points (1-sided p-value <0.025).

| **Statistical analysis title** | Serotype 5 |
|---|---|
| Statistical analysis description: | |
| Participants With IgG ≥0.35 µg/mL | |
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 682 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority[12] |
| P-value | < 0.001 |
| Method | Miettinen and Nurminen |
| Parameter estimate | Difference in Percent |
| Point estimate | -1.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3 |
| upper limit | -0.1 |

Notes:

[12] - The stratum-adjusted proportion difference using the Cochran-Mantel-Haenszel weight, and the corresponding 95% CI and p-value based on the method of Miettinen and Nurminen stratified by age category (2 months of age, ≥3 months of age). A conclusion of non-inferiority of V114 to PCV13 is based on the lower bound of the 2-sided 95% CI for the difference in percentages (V114 - PCV13) being >-10 percentage points (1-sided p-value <0.025).

| **Statistical analysis title** | Serotype 6A |
|---|---|
| Statistical analysis description: | |
| Participants With IgG ≥0.35 µg/mL | |
| Comparison groups | V114 v PCV13 |

| | |
|---|---|
| Number of subjects included in analysis | 682 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority[13] |
| P-value | < 0.001 |
| Method | Miettinen and Nurminen |
| Parameter estimate | Difference in Percent |
| Point estimate | -0.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.6 |
| upper limit | 0.2 |

Notes:

[13] - The stratum-adjusted proportion difference using the Cochran-Mantel-Haenszel weight, and the corresponding 95% CI and p-value based on the method of Miettinen and Nurminen stratified by age category (2 months of age, ≥3 months of age). A conclusion of non-inferiority of V114 to PCV13 is based on the lower bound of the 2-sided 95% CI for the difference in percentages (V114 - PCV13) being >-10 percentage points (1-sided p-value <0.025).

| **Statistical analysis title** | Serotype 6B |
|---|---|
| Statistical analysis description: | |
| Participants With IgG ≥0.35 µg/mL | |
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 682 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority[14] |
| P-value | < 0.001 |
| Method | Miettinen and Nurminen |
| Parameter estimate | Difference in Percent |
| Point estimate | -3.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -6.9 |
| upper limit | -1.3 |

Notes:

[14] - The stratum-adjusted proportion difference using the Cochran-Mantel-Haenszel weight, and the corresponding 95% CI and p-value based on the method of Miettinen and Nurminen stratified by age category (2 months of age, ≥3 months of age). A conclusion of non-inferiority of V114 to PCV13 is based on the lower bound of the 2-sided 95% CI for the difference in percentages (V114 - PCV13) being >-10 percentage points (1-sided p-value <0.025).

| **Statistical analysis title** | Serotype 7F |
|---|---|
| Statistical analysis description: | |
| Participants With IgG ≥0.35 µg/mL | |
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 682 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority[15] |
| P-value | < 0.001 |
| Method | Miettinen and Nurminen |
| Parameter estimate | Difference in Percent |
| Point estimate | -0.3 |

| | |
|---|---|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.7 |
| upper limit | 0.8 |

Notes:

[15] - The stratum-adjusted proportion difference using the Cochran-Mantel-Haenszel weight, and the corresponding 95% CI and p-value based on the method of Miettinen and Nurminen stratified by age category (2 months of age, ≥3 months of age). A conclusion of non-inferiority of V114 to PCV13 is based on the lower bound of the 2-sided 95% CI for the difference in percentages (V114 - PCV13) being >-10 percentage points (1-sided p-value <0.025).

| **Statistical analysis title** | Serotype 9V |
|---|---|
| Statistical analysis description: | |
| Participants With IgG ≥0.35 µg/mL | |
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 682 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority[16] |
| P-value | < 0.001 |
| Method | Miettinen and Nurminen |
| Parameter estimate | Difference in Percent |
| Point estimate | -0.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.7 |
| upper limit | 0.8 |

Notes:

[16] - The stratum-adjusted proportion difference using the Cochran-Mantel-Haenszel weight, and the corresponding 95% CI and p-value based on the method of Miettinen and Nurminen stratified by age category (2 months of age, ≥3 months of age). A conclusion of non-inferiority of V114 to PCV13 is based on the lower bound of the 2-sided 95% CI for the difference in percentages (V114 - PCV13) being >-10 percentage points (1-sided p-value <0.025).

| **Statistical analysis title** | Serotype 14 |
|---|---|
| Statistical analysis description: | |
| Participants With IgG ≥0.35 µg/mL | |
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 682 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority[17] |
| P-value | < 0.001 |
| Method | Miettinen and Nurminen |
| Parameter estimate | Difference in Percent |
| Point estimate | -0.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.9 |
| upper limit | 1.1 |

Notes:

[17] - The stratum-adjusted proportion difference using the Cochran-Mantel-Haenszel weight, and the corresponding 95% CI and p-value based on the method of Miettinen and Nurminen stratified by age category (2 months of age, ≥3 months of age). A conclusion of non-inferiority of V114 to PCV13 is

based on the lower bound of the 2-sided 95% CI for the difference in percentages (V114 - PCV13) being >-10 percentage points (1-sided p-value <0.025).

| **Statistical analysis title** | Serotype 18C |
|---|---|
| Statistical analysis description: | |
| Participants With IgG ≥0.35 µg/mL | |
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 682 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority[18] |
| P-value | < 0.001 |
| Method | Miettinen and Nurminen |
| Parameter estimate | Difference in Percent |
| Point estimate | -1.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3 |
| upper limit | -0.1 |

Notes:

[18] - The stratum-adjusted proportion difference using the Cochran-Mantel-Haenszel weight, and the corresponding 95% CI and p-value based on the method of Miettinen and Nurminen stratified by age category (2 months of age, ≥3 months of age). A conclusion of non-inferiority of V114 to PCV13 is based on the lower bound of the 2-sided 95% CI for the difference in percentages (V114 - PCV13) being >-10 percentage points (1-sided p-value <0.025).

| **Statistical analysis title** | Serotype 19A |
|---|---|
| Statistical analysis description: | |
| Participants With IgG ≥0.35 µg/mL | |
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 682 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority[19] |
| P-value | < 0.001 |
| Method | Miettinen and Nurminen |
| Parameter estimate | Difference in Percent |
| Point estimate | -0.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.7 |
| upper limit | 0.8 |

Notes:

[19] - The stratum-adjusted proportion difference using the Cochran-Mantel-Haenszel weight, and the corresponding 95% CI and p-value based on the method of Miettinen and Nurminen stratified by age category (2 months of age, ≥3 months of age). A conclusion of non-inferiority of V114 to PCV13 is based on the lower bound of the 2-sided 95% CI for the difference in percentages (V114 - PCV13) being >-10 percentage points (1-sided p-value <0.025).

| **Statistical analysis title** | Serotype 19F |
|---|---|
| Statistical analysis description: | |
| Participants With IgG ≥0.35 µg/mL | |
| Comparison groups | V114 v PCV13 |

| | |
|---|---|
| Number of subjects included in analysis | 682 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority[20] |
| P-value | < 0.001 |
| Method | Miettinen and Nurminen |
| Parameter estimate | Difference in Percent |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.1 |
| upper limit | 1.1 |

Notes:

[20] - The stratum-adjusted proportion difference using the Cochran-Mantel-Haenszel weight, and the corresponding 95% CI and p-value based on the method of Miettinen and Nurminen stratified by age category (2 months of age, ≥3 months of age). A conclusion of non-inferiority of V114 to PCV13 is based on the lower bound of the 2-sided 95% CI for the difference in percentages (V114 - PCV13) being >-10 percentage points (1-sided p-value <0.025).

| **Statistical analysis title** | Serotype 23F |
|---|---|
| Statistical analysis description: | |
| Participants With IgG ≥0.35 µg/mL | |
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 682 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority[21] |
| P-value | < 0.001 |
| Method | Miettinen and Nurminen |
| Parameter estimate | Difference in Percent |
| Point estimate | -1.8 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -4 |
| upper limit | -0.2 |

Notes:

[21] - The stratum-adjusted proportion difference using the Cochran-Mantel-Haenszel weight, and the corresponding 95%
CI and p-value based on the method of Miettinen and Nurminen stratified by age category (2 months of age, ≥3
months of age). A conclusion of non-inferiority of V114 to PCV13 is based on the lower bound of the 2-sided 95% CI for the difference in percentages (V114 - PCV13) being >-10 percentage points (1-sided p-value <0.025).

| **Statistical analysis title** | Serotype 22F |
|---|---|
| Statistical analysis description: | |
| Participants With IgG ≥0.35 µg/mL | |
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 682 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority[22] |
| P-value | < 0.001 |
| Method | Miettinen and Nurminen |
| Parameter estimate | Difference in Percent |
| Point estimate | 2 |

| | |
|---|---|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.4 |
| upper limit | 4.3 |

Notes:

[22] - The stratum-adjusted proportion difference using the Cochran-Mantel-Haenszel weight, and the corresponding 95% CI and p-value based on the method of Miettinen and Nurminen stratified by age category (2 months of age, ≥3 months of age). A conclusion of non-inferiority of V114 to PCV13 is based on the lower bound of the 2-sided 95% CI for the difference in percentages (V114 - PCV13) being >-10 percentage points (1-sided p-value <0.025).

| **Statistical analysis title** | Serotype 33F |
|---|---|

Statistical analysis description:

Participants With IgG ≥0.35 µg/mL

| | |
|---|---|
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 682 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority[23] |
| P-value | = 0.048 |
| Method | Miettinen and Nurminen |
| Parameter estimate | Difference in Percent |
| Point estimate | -6.8 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -10.6 |
| upper limit | -3.5 |

Notes:

[23] - The stratum-adjusted proportion difference using the Cochran-Mantel-Haenszel weight, and the corresponding 95% CI and p-value based on the method of Miettinen and Nurminen stratified by age category (2 months of age, ≥3 months of age). A conclusion of non-inferiority of V114 to PCV13 is based on the lower bound of the 2-sided 95% CI for the difference in percentages (V114 - PCV13) being >-10 percentage points (1-sided p-value <0.025).

## Primary: Geometric Mean Concentration of Serotype-Specific IgG for the 13 Shared Serotypes in V114 and PCV13 After Dose 3

| End point title | Geometric Mean Concentration of Serotype-Specific IgG for the 13 Shared Serotypes in V114 and PCV13 After Dose 3 |
|---|---|

End point description:

The anti-PnPs serotype-specific IgG Geometric Mean Concentrations (GMCs) of participants administered V114 versus participants administered PCV13 for the 13 serotypes shared in V114 and PCV13 were determined using an electrochemiluminescence assay. All randomized participants without protocol deviations that could have substantially impacted the results of the immunogenicity endpoint and who had sufficient data to perform the analyses were analyzed. One participant in the PCV13 group did not receive PCV13 and therefore was not included in the analysis for this end point.

| End point type | Primary |
|---|---|

End point timeframe:

30 Days after Dose 3, up to a total of 11 months

| End point values | V114 | PCV13 | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 339 | 343 | | |
| Units: µg/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Serotype 1 (Shared) (n=339, 343) | 2.39 (2.19 to 2.62) | 3.95 (3.61 to 4.32) | | |
| Serotype 3 (Shared) (n=339, 343) | 2.63 (2.39 to 2.89) | 1.42 (1.29 to 1.56) | | |
| Serotype 4 (Shared) (n=339, 343) | 2.98 (2.71 to 3.27) | 3.54 (3.23 to 3.89) | | |
| Serotype 5 (Shared) (n=338, 343) | 2.59 (2.32 to 2.89) | 3.35 (3.00 to 3.74) | | |
| Serotype 6A (Shared) (n=339, 343) | 2.51 (2.26 to 2.79) | 4.45 (4.00 to 4.94) | | |
| Serotype 6B (Shared) (n=339, 343) | 2.46 (2.14 to 2.82) | 4.17 (3.63 to 4.79) | | |
| Serotype 7F (Shared) (n=339, 343) | 4.38 (3.95 to 4.85) | 5.22 (4.71 to 5.78) | | |
| Serotype 9V (Shared) (n=339, 343) | 3.09 (2.80 to 3.41) | 3.55 (3.22 to 3.92) | | |
| Serotype 14 (Shared) (n=339, 342) | 8.99 (7.96 to 10.14) | 12.03 (10.66 to 13.57) | | |
| Serotype 18C (Shared) (n=339, 343) | 2.85 (2.58 to 3.14) | 3.85 (3.49 to 4.25) | | |
| Serotype 19A (Shared) (n=339, 343) | 3.44 (3.14 to 3.77) | 5.28 (4.82 to 5.79) | | |
| Serotype 19F (Shared) (n=339, 343) | 4.24 (3.93 to 4.58) | 5.65 (5.24 to 6.10) | | |
| Serotype 23F (Shared) (n=338, 342) | 2.42 (2.15 to 2.72) | 2.95 (2.62 to 3.32) | | |

## Statistical analyses

| Statistical analysis title | Serotype 1 |
|---|---|
| Statistical analysis description: IgG GMC Ratio | |
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 682 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority[24] |
| P-value | < 0.001 |
| Method | Linear model |
| Parameter estimate | GMC Ratio |
| Point estimate | 0.61 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.55 |
| upper limit | 0.67 |

Notes:

[24] - Based on a linear model with natural log-transformed IgG concentrations as response variable, and vaccination group and age category (2 months of age, ≥3 months of age) as factors. A conclusion of non-inferiority of V114 to PCV13 is based on the lower bound of the 2-sided 95% CI for the GMC ratio (V114/PCV13) being >0.5 (1-sided p-value <0.025).

| **Statistical analysis title** | Serotype 3 |
|---|---|
| Statistical analysis description: | |
| IgG GMC Ratio | |
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 682 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority[25] |
| P-value | < 0.001 |
| Method | Linear model |
| Parameter estimate | GMC Ratio |
| Point estimate | 1.85 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.67 |
| upper limit | 2.05 |

Notes:

[25] - Based on a linear model with natural log-transformed IgG concentrations as response variable, and vaccination group and age category (2 months of age, ≥3 months of age) as factors. A conclusion of non-inferiority of V114 to PCV13 is based on the lower bound of the 2-sided 95% CI for the GMC ratio (V114/PCV13) being >0.5 (1-sided p-value <0.025).

| **Statistical analysis title** | Serotype 4 |
|---|---|
| Statistical analysis description: | |
| IgG GMC Ratio | |
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 682 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority[26] |
| P-value | < 0.001 |
| Method | Linear model |
| Parameter estimate | GMC Ratio |
| Point estimate | 0.84 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.76 |
| upper limit | 0.93 |

Notes:

[26] - Based on a linear model with natural log-transformed IgG concentrations as response variable, and vaccination group and age category (2 months of age, ≥3 months of age) as factors. A conclusion of non-inferiority of V114 to PCV13 is based on the lower bound of the 2-sided 95% CI for the GMC ratio (V114/PVC 13) being >0.5 (1-sided p-value <0.025).

| **Statistical analysis title** | Serotype 5 |
|---|---|
| Statistical analysis description: | |
| IgG GMC Ratio | |
| Comparison groups | V114 v PCV13 |

| | |
|---|---|
| Number of subjects included in analysis | 682 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority[27] |
| P-value | < 0.001 |
| Method | Linear model |
| Parameter estimate | GMC Ratio |
| Point estimate | 0.77 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.69 |
| upper limit | 0.87 |

Notes:

[27] - Based on a linear model with natural log-transformed IgG concentrations as response variable, and vaccination group and age category (2 months of age, ≥3 months of age) as factors. A conclusion of non-inferiority of V114 to PCV13 is based on the lower bound of the 2-sided 95% CI for the GMC ratio (V114/PVC 13) being >0.5 (1-sided p-value <0.025).

| **Statistical analysis title** | Serotype 6A |
|---|---|
| Statistical analysis description: | |
| IgG GMC Ratio | |
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 682 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority[28] |
| P-value | = 0.019 |
| Method | Linear model |
| Parameter estimate | GMC Ratio |
| Point estimate | 0.56 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.5 |
| upper limit | 0.63 |

Notes:

[28] - Based on a linear model with natural log-transformed IgG concentrations as response variable, and vaccination group and age category (2 months of age, ≥3 months of age) as factors. A conclusion of non-inferiority of V114 to PCV13 is based on the lower bound of the 2-sided 95% CI for the GMC ratio (V114/PVC 13) being >0.5 (1-sided p-value <0.025).

| **Statistical analysis title** | Serotype 6B |
|---|---|
| Statistical analysis description: | |
| IgG GMC Ratio | |
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 682 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority[29] |
| P-value | = 0.015 |
| Method | Linear model |
| Parameter estimate | GMC Ratio |
| Point estimate | 0.59 |

| | |
|---|---|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.51 |
| upper limit | 0.68 |

Notes:

[29] - Based on a linear model with natural log-transformed IgG concentrations as response variable, and vaccination group and age category (2 months of age, ≥3 months of age) as factors. A conclusion of non-inferiority of V114 to PCV13 is based on the lower bound of the 2-sided 95% CI for the GMC ratio (V114/PVC 13) being >0.5 (1-sided p-value <0.025).

| **Statistical analysis title** | Serotype 7F |
|---|---|

Statistical analysis description:

IgG GMC Ratio

| | |
|---|---|
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 682 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority[30] |
| P-value | < 0.001 |
| Method | Linear model |
| Parameter estimate | GMC Ratio |
| Point estimate | 0.84 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.75 |
| upper limit | 0.94 |

Notes:

[30] - Based on a linear model with natural log-transformed IgG concentrations as response variable, and vaccination group and age category (2 months of age, ≥3 months of age) as factors. A conclusion of non-inferiority of V114 to PCV13 is based on the lower bound of the 2-sided 95% CI for the GMC ratio (V114/PVC 13) being >0.5 (1-sided p-value <0.025).

| **Statistical analysis title** | Serotype 9V |
|---|---|

Statistical analysis description:

IgG GMC Ratio

| | |
|---|---|
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 682 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority[31] |
| P-value | < 0.001 |
| Method | Linear model |
| Parameter estimate | GMC Ratio |
| Point estimate | 0.87 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.78 |
| upper limit | 0.97 |

Notes:

[31] - Based on a linear model with natural log-transformed IgG concentrations as response variable, and vaccination group and age category (2 months of age, ≥3 months of age) as factors. A conclusion of non-inferiority of V114 to PCV13 is based on the lower bound of the 2-sided 95% CI for the GMC ratio (V114/PVC 13) being >0.5 (1-sided p-value <0.025).

| **Statistical analysis title** | Serotype 14 |
|---|---|
| Statistical analysis description: | |
| IgG GMC Ratio | |
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 682 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority[32] |
| P-value | < 0.001 |
| Method | Linear model |
| Parameter estimate | GMC Ratio |
| Point estimate | 0.75 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.66 |
| upper limit | 0.85 |

Notes:

[32] - Based on a linear model with natural log-transformed IgG concentrations as response variable, and vaccination group and age category (2 months of age, ≥3 months of age) as factors. A conclusion of non-inferiority of V114 to PCV13 is based on the lower bound of the 2-sided 95% CI for the GMC ratio (V114/PVC 13) being >0.5 (1-sided p-value <0.025).

| **Statistical analysis title** | Serotype 18C |
|---|---|
| Statistical analysis description: | |
| IgG GMC Ratio | |
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 682 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority[33] |
| P-value | < 0.001 |
| Method | Linear model |
| Parameter estimate | GMC Ratio |
| Point estimate | 0.74 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.67 |
| upper limit | 0.82 |

Notes:

[33] - Based on a linear model with natural log-transformed IgG concentrations as response variable, and vaccination group and age category (2 months of age, ≥3 months of age) as factors. A conclusion of non-inferiority of V114 to PCV13 is based on the lower bound of the 2-sided 95% CI for the GMC ratio (V114/PVC 13) being >0.5 (1-sided p-value <0.025).

| **Statistical analysis title** | Serotype 19A |
|---|---|
| Statistical analysis description: | |
| IgG GMC Ratio | |
| Comparison groups | V114 v PCV13 |

| | |
|---|---|
| Number of subjects included in analysis | 682 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority[34] |
| P-value | < 0.001 |
| Method | Linear model |
| Parameter estimate | GMC Ratio |
| Point estimate | 0.65 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.59 |
| upper limit | 0.72 |

Notes:

[34] - Based on a linear model with natural log-transformed IgG concentrations as response variable, and vaccination group and age category (2 months of age, ≥3 months of age) as factors. A conclusion of non-inferiority of V114 to PCV13 is based on the lower bound of the 2-sided 95% CI for the GMC ratio (V114/PVC 13) being >0.5 (1-sided p-value <0.025).

| **Statistical analysis title** | Serotype 19F |
|---|---|
| Statistical analysis description: | |
| IgG GMC Ratio | |
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 682 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority[35] |
| P-value | < 0.001 |
| Method | Linear model |
| Parameter estimate | GMC Ratio |
| Point estimate | 0.75 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.69 |
| upper limit | 0.82 |

Notes:

[35] - Based on a linear model with natural log-transformed IgG concentrations as response variable, and vaccination group and age category (2 months of age, ≥3 months of age) as factors. A conclusion of non-inferiority of V114 to PCV13 is based on the lower bound of the 2-sided 95% CI for the GMC ratio (V114/PVC 13) being >0.5 (1-sided p-value <0.025).

| **Statistical analysis title** | Serotype 23F |
|---|---|
| Statistical analysis description: | |
| IgG GMC Ratio | |
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 682 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority[36] |
| P-value | < 0.001 |
| Method | Linear model |
| Parameter estimate | GMC Ratio |
| Point estimate | 0.82 |

| | |
|---|---|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.72 |
| upper limit | 0.93 |

Notes:

[36] - Based on a linear model with natural log-transformed IgG concentrations as response variable, and vaccination group and age category (2 months of age, ≥3 months of age) as factors. A conclusion of non-inferiority of V114 to PCV13 is based on the lower bound of the 2-sided 95% CI for the GMC ratio (V114/PVC 13) being >0.5 (1-sided p-value <0.025).

## Secondary: GMC of Serotype-Specific IgG for the 2 Unique V114 Serotypes After Dose 3

| | |
|---|---|
| End point title | GMC of Serotype-Specific IgG for the 2 Unique V114 Serotypes After Dose 3 |

End point description:

The anti-PnPs serotype-specific IgG GMCs of participants administered V114 versus participants administered PCV13 for the 2 unique V114 serotypes was determined using an electrochemiluminescence assay. All randomized participants without protocol deviations that could have substantially impacted the results of the immunogenicity endpoint and who had sufficient data to perform the analyses were analyzed. One participant in the PCV13 group did not receive PCV13 and therefore was not included in the analysis for this end point.

| | |
|---|---|
| End point type | Secondary |

End point timeframe:

30 days after Dose 3, up to a total of 11 months

| End point values | V114 | PCV13 | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 339 | 343 | | |
| Units: µg/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Serotype 22F (Unique to V114) (n=339, 343) | 6.59 (5.95 to 7.30) | 0.06 (0.06 to 0.07) | | |
| Serotype 33F (Unique to V114) (n=339, 337) | 1.85 (1.60 to 2.14) | 0.06 (0.05 to 0.07) | | |

## Statistical analyses

| Statistical analysis title | Serotype 22F |
|---|---|

Statistical analysis description:

IgG GMC Ratio

| | |
|---|---|
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 682 |
| Analysis specification | Pre-specified |
| Analysis type | other[37] |
| Parameter estimate | GMC Ratio |
| Point estimate | 107.45 |

| | |
|---|---|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 96.18 |
| upper limit | 120.03 |

Notes:

[37] - Based on a linear model with natural log-transformed IgG concentrations as response variable, and vaccination group and age category (2 months of age, ≥3 months of age) as factors.

| **Statistical analysis title** | Serotype 33F |
|---|---|

Statistical analysis description:

IgG GMC Ratio

| | |
|---|---|
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 682 |
| Analysis specification | Pre-specified |
| Analysis type | other[38] |
| Parameter estimate | GMC Ratio |
| Point estimate | 32.48 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 27.72 |
| upper limit | 38.05 |

Notes:

[38] - Based on a linear model with natural log-transformed IgG concentrations as response variable, and vaccination group and age category (2 months of age, ≥3 months of age) as factors.

## Secondary: Percentage of Participants Meeting the Serotype Specific IgG Threshold Value of ≥0.35 µg/mL for Each Serotype in V114 After Dose 4

| | |
|---|---|
| End point title | Percentage of Participants Meeting the Serotype Specific IgG Threshold Value of ≥0.35 µg/mL for Each Serotype in V114 After Dose 4 |

End point description:

The anti-PnPs serotype-specific IgG response rates (percentage of participants meeting serotype-specific IgG threshold value of ≥0.35 µg/mL for participants administered V114 versus participants administered PCV13) for the 15 serotypes contained in V114 were determined using an electrochemiluminescence assay. All randomized participants without protocol deviations that could have substantially impacted the results of the immunogenicity endpoint and who had sufficient data to perform the analyses were analyzed. One participant in the PCV13 group did not receive PCV13 and therefore was not included in the analysis for this end point.

| | |
|---|---|
| End point type | Secondary |

End point timeframe:

30 Days after Dose 4, up to a total of 14 months

| **End point values** | V114 | PCV13 | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 333 | 334 | | |
| Units: Percentage of Participants | | | | |
| number (not applicable) | | | | |
| Serotype 1 (Shared) (n=333, 334) | 99.7 | 100.0 | | |
| Serotype 3 (Shared) (n=333, 334) | 100.0 | 96.7 | | |
| Serotype 4 (Shared) (n=333, 334) | 99.7 | 100.0 | | |

| | | | | |
|---|---|---|---|---|
| Serotype 5 (Shared) (n=333, 334) | 100.0 | 100.0 | | |
| Serotype 6A (Shared) (n=333, 334) | 100.0 | 100.0 | | |
| Serotype 6B (Shared) (n=333, 334) | 100.0 | 100.0 | | |
| Serotype 7F (Shared) (n=333, 334) | 100.0 | 100.0 | | |
| Serotype 9V (Shared) (n=333, 334) | 100.0 | 100.0 | | |
| Serotype 14 (Shared) (n=333, 334) | 100.0 | 100.0 | | |
| Serotype 18C (Shared) (n=333, 334) | 100.0 | 100.0 | | |
| Serotype 19A (Shared) (n=333, 334) | 100.0 | 100.0 | | |
| Serotype 19F (Shared) (n=333, 334) | 100.0 | 100.0 | | |
| Serotype 23F (Shared) (n=332, 334) | 99.7 | 99.4 | | |
| Serotype 22F (Unique to V114) (n=333, 327) | 100.0 | 5.2 | | |
| Serotype 33F (Unique to V114) (n=333, 313) | 100.0 | 11.5 | | |

## Statistical analyses

| **Statistical analysis title** | Serotype 1 |
|---|---|
| Statistical analysis description: | |
| Participants With IgG ≥0.35 µg/mL | |
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 667 |
| Analysis specification | Pre-specified |
| Analysis type | other[39] |
| Parameter estimate | Difference in Percent |
| Point estimate | -0.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.7 |
| upper limit | 0.8 |

Notes:

[39] - The stratum-adjusted proportion difference using the Cochran-Mantel-Haenszel weight, and the corresponding 95% CI based on the method of Miettinen and Nurminen stratified by age category (2 months of age, ≥3 months of age).

| **Statistical analysis title** | Serotype 3 |
|---|---|
| Statistical analysis description: | |
| Participants With IgG ≥0.35 µg/mL | |
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 667 |
| Analysis specification | Pre-specified |
| Analysis type | other[40] |
| Parameter estimate | Difference in Percent |
| Point estimate | 3.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.8 |
| upper limit | 5.8 |

Notes:

[40] - The stratum-adjusted proportion difference using the Cochran-Mantel-Haenszel weight, and the corresponding 95% CI based on the method of Miettinen and Nurminen stratified by age category (2 months of age, ≥3 months of age).

| **Statistical analysis title** | Serotype 4 |
|---|---|
| Statistical analysis description: | |
| Participants With IgG ≥0.35 µg/mL | |
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 667 |
| Analysis specification | Pre-specified |
| Analysis type | other[41] |
| Parameter estimate | Difference in Percent |
| Point estimate | -0.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.7 |
| upper limit | 0.8 |

Notes:

[41] - The stratum-adjusted proportion difference using the Cochran-Mantel-Haenszel weight, and the corresponding 95% CI based on the method of Miettinen and Nurminen stratified by age category (2 months of age, ≥3 months of age).

| **Statistical analysis title** | Serotype 5 |
|---|---|
| Statistical analysis description: | |
| Participants With IgG ≥0.35 µg/mL | |
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 667 |
| Analysis specification | Pre-specified |
| Analysis type | other[42] |
| Parameter estimate | Difference in Percent |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.1 |
| upper limit | 1.1 |

Notes:

[42] - The stratum-adjusted proportion difference using the Cochran-Mantel-Haenszel weight, and the corresponding 95% CI based on the method of Miettinen and Nurminen stratified by age category (2 months of age, ≥3 months of age).

| **Statistical analysis title** | Serotype 6A |
|---|---|
| Statistical analysis description: | |
| Participants With IgG ≥0.35 µg/mL | |
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 667 |
| Analysis specification | Pre-specified |
| Analysis type | other[43] |
| Parameter estimate | Difference in Percent |
| Point estimate | 0 |

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

Notes:

[43] - The stratum-adjusted proportion difference using the Cochran-Mantel-Haenszel weight, and the corresponding 95% CI based on the method of Miettinen and Nurminen stratified by age category (2 months of age, ≥3 months of age).

| **Statistical analysis title** | Serotype 6B |
|---|---|
| Statistical analysis description: | |
| Participants With IgG ≥0.35 µg/mL | |
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 667 |
| Analysis specification | Pre-specified |
| Analysis type | other[44] |
| Parameter estimate | Difference in Percent |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.1 |
| upper limit | 1.1 |

Notes:

[44] - The stratum-adjusted proportion difference using the Cochran-Mantel-Haenszel weight, and the corresponding 95% CI based on the method of Miettinen and Nurminen stratified by age category (2 months of age, ≥3 months of age).

| **Statistical analysis title** | Serotype 7F |
|---|---|
| Statistical analysis description: | |
| Participants With IgG ≥0.35 µg/mL | |
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 667 |
| Analysis specification | Pre-specified |
| Analysis type | other[45] |
| Parameter estimate | Difference in Percent |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.1 |
| upper limit | 1.1 |

Notes:

[45] - The stratum-adjusted proportion difference using the Cochran-Mantel-Haenszel weight, and the corresponding 95% CI based on the method of Miettinen and Nurminen stratified by age category (2 months of age, ≥3 months of age).

| **Statistical analysis title** | Serotype 9V |
|---|---|
| Statistical analysis description: | |
| Participants With IgG ≥0.35 µg/mL | |
| Comparison groups | V114 v PCV13 |

| | |
|---|---|
| Number of subjects included in analysis | 667 |
| Analysis specification | Pre-specified |
| Analysis type | other[46] |
| Parameter estimate | Difference in Percent |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.1 |
| upper limit | 1.1 |

Notes:

[46] - The stratum-adjusted proportion difference using the Cochran-Mantel-Haenszel weight, and the corresponding 95% CI based on the method of Miettinen and Nurminen stratified by age category (2 months of age, ≥3 months of age).

| **Statistical analysis title** | Serotype 14 |
|---|---|

Statistical analysis description:

Participants With IgG ≥0.35 µg/mL

| | |
|---|---|
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 667 |
| Analysis specification | Pre-specified |
| Analysis type | other[47] |
| Parameter estimate | Difference in Percent |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.1 |
| upper limit | 1.1 |

Notes:

[47] - The stratum-adjusted proportion difference using the Cochran-Mantel-Haenszel weight, and the corresponding 95% CI based on the method of Miettinen and Nurminen stratified by age category (2 months of age, ≥3 months of age).

| **Statistical analysis title** | Serotype 18C |
|---|---|

Statistical analysis description:

Participants With IgG ≥0.35 µg/mL

| | |
|---|---|
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 667 |
| Analysis specification | Pre-specified |
| Analysis type | other[48] |
| Parameter estimate | Difference in Percent |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.1 |
| upper limit | 1.1 |

Notes:

[48] - The stratum-adjusted proportion difference using the Cochran-Mantel-Haenszel weight, and the corresponding 95% CI based on the method of Miettinen and Nurminen stratified by age category (2 months of age, ≥3 months of age).

| **Statistical analysis title** | Serotype 19A |
|---|---|

| | |
|---|---|
| Statistical analysis description: | |
| Participants With IgG ≥0.35 µg/mL | |
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 667 |
| Analysis specification | Pre-specified |
| Analysis type | other[49] |
| Parameter estimate | Difference in Percent |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.1 |
| upper limit | 1.1 |

Notes:

[49] - The stratum-adjusted proportion difference using the Cochran-Mantel-Haenszel weight, and the corresponding 95% CI based on the method of Miettinen and Nurminen stratified by age category (2 months of age, ≥3 months of age).

| **Statistical analysis title** | Serotype 19F |
|---|---|
| Statistical analysis description: | |
| Participants With IgG ≥0.35 µg/mL | |
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 667 |
| Analysis specification | Pre-specified |
| Analysis type | other[50] |
| Parameter estimate | Difference in Percent |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.1 |
| upper limit | 1.1 |

Notes:

[50] - The stratum-adjusted proportion difference using the Cochran-Mantel-Haenszel weight, and the corresponding 95% CI based on the method of Miettinen and Nurminen stratified by age category (2 months of age, ≥3 months of age).

| **Statistical analysis title** | Serotype 23F |
|---|---|
| Statistical analysis description: | |
| Participants With IgG ≥0.35 µg/mL | |
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 667 |
| Analysis specification | Pre-specified |
| Analysis type | other[51] |
| Parameter estimate | Difference in Percent |
| Point estimate | 0.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.1 |
| upper limit | 1.9 |

Notes:

[51] - The stratum-adjusted proportion difference using the Cochran-Mantel-Haenszel weight, and the corresponding 95% CI based on the method of Miettinen and Nurminen stratified by age category (2 months of age, ≥3 months of age).

| **Statistical analysis title** | Serotype 22F |
|---|---|
| Statistical analysis description: | |
| Participants With IgG ≥0.35 µg/mL | |
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 667 |
| Analysis specification | Pre-specified |
| Analysis type | other[52] |
| Parameter estimate | Difference in Percent |
| Point estimate | 94.8 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 91.8 |
| upper limit | 96.7 |

Notes:

[52] - The stratum-adjusted proportion difference using the Cochran-Mantel-Haenszel weight, and the corresponding 95% CI based on the method of Miettinen and Nurminen stratified by age category (2 months of age, ≥3 months of age).

| **Statistical analysis title** | Serotype 33F |
|---|---|
| Statistical analysis description: | |
| Participants With IgG ≥0.35 µg/mL | |
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 667 |
| Analysis specification | Pre-specified |
| Analysis type | other[53] |
| Parameter estimate | Difference in Percent |
| Point estimate | 88.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 84.5 |
| upper limit | 91.6 |

Notes:

[53] - The stratum-adjusted proportion difference using the Cochran-Mantel-Haenszel weight, and the corresponding 95% CI based on the method of Miettinen and Nurminen stratified by age category (2 months of age, ≥3 months of age).

## Secondary: GMC of Serotype-Specific IgG for Each Serotype in V114 After Dose 4

| End point title | GMC of Serotype-Specific IgG for Each Serotype in V114 After Dose 4 |
|---|---|

End point description:

The anti-PnPs serotype-specific IgG GMCs of participants administered V114 versus participants administered PCV13 for the 15 serotypes contained in V114 was determined using an electrochemiluminescence assay. All randomized participants without protocol deviations that could have substantially impacted the results of the immunogenicity endpoint and who had sufficient data to perform the analyses were analyzed. One participant in the PCV13 group did not receive PCV13 and therefore was not included in the analysis for this end point.

| End point type | Secondary |
|---|---|

End point timeframe:

30 Days after Dose 4, up to a total of 14 months

| End point values | V114 | PCV13 | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 333 | 334 | | |
| Units: µg/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Serotype 1 (Shared) (n=333, 334) | 2.74 (2.47 to 3.04) | 5.19 (4.68 to 5.77) | | |
| Serotype 3 (Shared) (n=333, 334) | 2.18 (1.97 to 2.41) | 1.28 (1.15 to 1.41) | | |
| Serotype 4 (Shared) (n=333, 334) | 2.91 (2.57 to 3.30) | 3.18 (2.81 to 3.59) | | |
| Serotype 5 (Shared) (n=333, 334) | 4.43 (3.96 to 4.95) | 6.65 (5.95 to 7.43) | | |
| Serotype 6A (Shared) (n=333, 334) | 6.05 (5.36 to 6.81) | 9.41 (8.35 to 10.60) | | |
| Serotype 6B (Shared) (n=333, 334) | 8.03 (7.12 to 9.05) | 10.88 (9.66 to 12.26) | | |
| Serotype 7F (Shared) (n=333, 334) | 5.80 (5.15 to 6.54) | 7.15 (6.35 to 8.05) | | |
| Serotype 9V (Shared) (n=333, 334) | 4.27 (3.79 to 4.81) | 5.18 (4.60 to 5.83) | | |
| Serotype 14 (Shared) (n=333, 334) | 9.51 (8.45 to 10.69) | 11.26 (10.02 to 12.66) | | |
| Serotype 18C (Shared) (n=333, 334) | 5.21 (4.60 to 5.89) | 5.21 (4.61 to 5.90) | | |
| Serotype 19A (Shared) (n=333, 334) | 6.88 (6.20 to 7.63) | 8.37 (7.55 to 9.28) | | |
| Serotype 19F (Shared) (n=333, 334) | 6.53 (5.89 to 7.22) | 7.76 (7.01 to 8.58) | | |
| Serotype 23F (Shared) (n=332, 334) | 3.75 (3.26 to 4.31) | 6.22 (5.42 to 7.15) | | |
| Serotype 22F (Unique to V114) (n=333, 327) | 11.42 (10.31 to 12.66) | 0.13 (0.12 to 0.15) | | |
| Serotype 33F (Unique to V114) (n=333, 313) | 6.14 (5.48 to 6.89) | 0.14 (0.12 to 0.15) | | |

## Statistical analyses

| Statistical analysis title | Serotype 1 |
|---|---|
| Statistical analysis description:<br>IgG GMC Ratio | |
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 667 |
| Analysis specification | Pre-specified |
| Analysis type | other[54] |
| Parameter estimate | GMC Ratio |
| Point estimate | 0.53 |

| | |
|---|---|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.47 |
| upper limit | 0.59 |

Notes:

[54] - Based on a linear model with natural log-transformed IgG concentrations as response variable, and vaccination group and age category (2 months of age, ≥3 months of age) as factors.

| **Statistical analysis title** | Serotype 3 |
|---|---|

Statistical analysis description:

IgG GMC Ratio

| | |
|---|---|
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 667 |
| Analysis specification | Pre-specified |
| Analysis type | other[55] |
| Parameter estimate | GMC Ratio |
| Point estimate | 1.71 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.53 |
| upper limit | 1.9 |

Notes:

[55] - Based on a linear model with natural log-transformed IgG concentrations as response variable, and vaccination group and age category (2 months of age, ≥3 months of age) as factors.

| **Statistical analysis title** | Serotype 4 |
|---|---|

Statistical analysis description:

IgG GMC Ratio

| | |
|---|---|
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 667 |
| Analysis specification | Pre-specified |
| Analysis type | other[56] |
| Parameter estimate | GMC Ratio |
| Point estimate | 0.92 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.8 |
| upper limit | 1.05 |

Notes:

[56] - Based on a linear model with natural log-transformed IgG concentrations as response variable, and vaccination group and age category (2 months of age, ≥3 months of age) as factors.

| **Statistical analysis title** | Serotype 5 |
|---|---|

Statistical analysis description:

IgG GMC Ratio

| | |
|---|---|
| Comparison groups | V114 v PCV13 |

| | |
|---|---|
| Number of subjects included in analysis | 667 |
| Analysis specification | Pre-specified |
| Analysis type | other[57] |
| Parameter estimate | GMC Ratio |
| Point estimate | 0.67 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.59 |
| upper limit | 0.75 |

Notes:

[57] - Based on a linear model with natural log-transformed IgG concentrations as response variable, and vaccination group and age category (2 months of age, ≥3 months of age) as factors.

| **Statistical analysis title** | Serotype 6A |
|---|---|

Statistical analysis description:

IgG GMC Ratio

| | |
|---|---|
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 667 |
| Analysis specification | Pre-specified |
| Analysis type | other[58] |
| Parameter estimate | GMC Ratio |
| Point estimate | 0.64 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.56 |
| upper limit | 0.73 |

Notes:

[58] - Based on a linear model with natural log-transformed IgG concentrations as response variable, and vaccination group and age category (2 months of age, ≥3 months of age) as factors.

| **Statistical analysis title** | Serotype 6B |
|---|---|

Statistical analysis description:

IgG GMC Ratio

| | |
|---|---|
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 667 |
| Analysis specification | Pre-specified |
| Analysis type | other[59] |
| Parameter estimate | GMC Ratio |
| Point estimate | 0.74 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.65 |
| upper limit | 0.84 |

Notes:

[59] - Based on a linear model with natural log-transformed IgG concentrations as response variable, and vaccination group and age category (2 months of age, ≥3 months of age) as factors.

| **Statistical analysis title** | Serotype 7F |
|---|---|

Statistical analysis description:

IgG GMC Ratio

| | |
|---|---|
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 667 |
| Analysis specification | Pre-specified |
| Analysis type | other[60] |
| Parameter estimate | GMC Ratio |
| Point estimate | 0.81 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.71 |
| upper limit | 0.92 |

Notes:

[60] - Based on a linear model with natural log-transformed IgG concentrations as response variable, and vaccination group and age category (2 months of age, ≥3 months of age) as factors.

| **Statistical analysis title** | Serotype 9V |
|---|---|
| Statistical analysis description: | |
| IgG GMC Ratio | |
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 667 |
| Analysis specification | Pre-specified |
| Analysis type | other[61] |
| Parameter estimate | GMC Ratio |
| Point estimate | 0.83 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.73 |
| upper limit | 0.94 |

Notes:

[61] - Based on a linear model with natural log-transformed IgG concentrations as response variable, and vaccination group and age category (2 months of age, ≥3 months of age) as factors.

| **Statistical analysis title** | Serotype 14 |
|---|---|
| Statistical analysis description: | |
| IgG GMC Ratio | |
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 667 |
| Analysis specification | Pre-specified |
| Analysis type | other[62] |
| Parameter estimate | GMC Ratio |
| Point estimate | 0.84 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.74 |
| upper limit | 0.96 |

Notes:

[62] - Based on a linear model with natural log-transformed IgG concentrations as response variable, and vaccination group and age category (2 months of age, ≥3 months of age) as factors.

| **Statistical analysis title** | Serotype 18C |
|---|---|

| Statistical analysis description: | |
|---|---|
| IgG GMC Ratio | |
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 667 |
| Analysis specification | Pre-specified |
| Analysis type | other[63] |
| Parameter estimate | GMC Ratio |
| Point estimate | 1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.87 |
| upper limit | 1.14 |

Notes:

[63] - Based on a linear model with natural log-transformed IgG concentrations as response variable, and vaccination group and age category (2 months of age, ≥3 months of age) as factors.

| **Statistical analysis title** | Serotype 19A |
|---|---|
| Statistical analysis description: | |
| IgG GMC Ratio | |
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 667 |
| Analysis specification | Pre-specified |
| Analysis type | other[64] |
| Parameter estimate | GMC Ratio |
| Point estimate | 0.82 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.73 |
| upper limit | 0.92 |

Notes:

[64] - Based on a linear model with natural log-transformed IgG concentrations as response variable, and vaccination group and age category (2 months of age, ≥3 months of age) as factors.

| **Statistical analysis title** | Serotype 19F |
|---|---|
| Statistical analysis description: | |
| IgG GMC Ratio | |
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 667 |
| Analysis specification | Pre-specified |
| Analysis type | other[65] |
| Parameter estimate | GMC Ratio |
| Point estimate | 0.84 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.75 |
| upper limit | 0.94 |

Notes:

[65] - Based on a linear model with natural log-transformed IgG concentrations as response variable, and vaccination group and age category (2 months of age, ≥3 months of age) as factors.

| **Statistical analysis title** | Serotype 23F |
|---|---|
| Statistical analysis description: | |
| IgG GMC Ratio | |
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 667 |
| Analysis specification | Pre-specified |
| Analysis type | other[66] |
| Parameter estimate | GMC Ratio |
| Point estimate | 0.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.52 |
| upper limit | 0.7 |

Notes:

[66] - Based on a linear model with natural log-transformed IgG concentrations as response variable, and vaccination group and age category (2 months of age, ≥3 months of age) as factors.

| **Statistical analysis title** | Serotype 22F |
|---|---|
| Statistical analysis description: | |
| IgG GMC Ratio | |
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 667 |
| Analysis specification | Pre-specified |
| Analysis type | other[67] |
| Parameter estimate | GMC Ratio |
| Point estimate | 86.74 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 77.61 |
| upper limit | 96.95 |

Notes:

[67] - Based on a linear model with natural log-transformed IgG concentrations as response variable, and vaccination group and age category (2 months of age, ≥3 months of age) as factors.

| **Statistical analysis title** | Serotype 33F |
|---|---|
| Statistical analysis description: | |
| IgG GMC Ratio | |
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 667 |
| Analysis specification | Pre-specified |
| Analysis type | other[68] |
| Parameter estimate | GMC Ratio |
| Point estimate | 45.44 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 40.07 |
| upper limit | 51.54 |

Notes:

[68] - Based on a linear model with natural log-transformed IgG concentrations as response variable, and vaccination group and age category (2 months of age, ≥3 months of age) as factors.

## Secondary: Geometric Mean Titer of Serotype-Specific Opsonophagocytic Activity for Each Serotype in V114 After Dose 3

| End point title | Geometric Mean Titer of Serotype-Specific Opsonophagocytic Activity for Each Serotype in V114 After Dose 3 |
|---|---|

End point description:

The anti-PnPs serotype-specific opsonophagocytic activity (OPA) and geometric mean titers (GMTs) of participants administered V114 versus participants administered PCV13 for the 15 serotypes contained in V114 was determined using a multiplexed opsonophagocytic assay. All randomized participants without protocol deviations that could have substantially impacted the results of the immunogenicity endpoint and who had sufficient data to perform the analyses were analyzed. One participant in the PCV13 group did not receive PCV13 and therefore was not included in the analysis for this end point.

| End point type | Secondary |
|---|---|

End point timeframe:

30 Days after Dose 3, up to a total of 11 months

| **End point values** | V114 | PCV13 | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 337 | 340 | | |
| Units: Titer | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Serotype 1 (Shared) (n=336, 340) | 211.51 (180.48 to 247.86) | 322.44 (275.23 to 377.76) | | |
| Serotype 3 (Shared) (n=333, 336) | 660.68 (586.60 to 744.11) | 471.43 (418.48 to 531.08) | | |
| Serotype 4 (Shared) (n=334, 338) | 3984.87 (3537.66 to 4488.62) | 4118.16 (3656.82 to 4637.70) | | |
| Serotype 5 (Shared) (n=336, 339) | 1241.69 (1098.82 to 1403.14) | 1358.43 (1202.35 to 1534.79) | | |
| Serotype 6A (Shared) (n=334, 336) | 9124.96 (7894.53 to 10547.16) | 11956.64 (10340.85 to 13824.91) | | |
| Serotype 6B (Shared) (n=334, 338) | 8416.19 (7243.92 to 9778.18) | 10421.94 (8972.87 to 12105.02) | | |
| Serotype 7F (Shared) (n=334, 338) | 22324.41 (19365.68 to 25735.19) | 27396.28 (23771.84 to 31573.33) | | |
| Serotype 9V (Shared) (n=334, 338) | 2725.29 (2399.27 to 3095.62) | 3338.40 (2939.75 to 3791.11) | | |
| Serotype 14 (Shared) (n=334, 339) | 14175.13 (12024.73 to 16710.08) | 12288.35 (10433.90 to 14472.40) | | |
| Serotype 18C (Shared) (n=334, 339) | 3698.24 (3346.73 to 4086.66) | 3705.21 (3353.84 to 4093.39) | | |
| Serotype 19A (Shared) (n=335, 339) | 2709.90 (2418.02 to 3037.02) | 3961.10 (3535.23 to 4438.26) | | |

| | | | | |
|---|---|---|---|---|
| Serotype 19F (Shared) (n=334, 339) | 2371.39 (2141.38 to 2624.87) | 2541.27 (2297.18 to 2811.29) | | |
| Serotype 23F (Shared) (n=334, 340) | 11861.63 (10118.30 to 13905.32) | 18957.26 (16186.86 to 22201.82) | | |
| Serotype 22F (Unique to V114) (n=333, 333) | 5575.08 (4769.68 to 6516.47) | 9.95 (8.51 to 11.63) | | |
| Serotype 33F (Unique to V114) (n=333, 334) | 23888.79 (17632.59 to 32364.75) | 121.79 (89.73 to 165.32) | | |

**Statistical analyses**

| **Statistical analysis title** | Serotype 1 |
|---|---|
| Statistical analysis description: | |
| OPA GMT Ratio | |
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 677 |
| Analysis specification | Pre-specified |
| Analysis type | other[69] |
| Parameter estimate | GMT Ratio |
| Point estimate | 0.66 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.55 |
| upper limit | 0.78 |

Notes:

[69] - Based on a linear model with natural log-transformed OPA titers as response variable, and vaccination group and age
category (2 months of age, ≥3 months of age) as factors.

| **Statistical analysis title** | Serotype 3 |
|---|---|
| Statistical analysis description: | |
| OPA GMT Ratio | |
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 677 |
| Analysis specification | Pre-specified |
| Analysis type | other[70] |
| Parameter estimate | GMT Ratio |
| Point estimate | 1.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.23 |
| upper limit | 1.59 |

Notes:

[70] - Based on a linear model with natural log-transformed OPA titers as response variable, and vaccination group and age
category (2 months of age, ≥3 months of age) as factors.

| **Statistical analysis title** | Serotype 4 |
|---|---|
| Statistical analysis description: | |
| OPA GMT Ratio | |
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 677 |
| Analysis specification | Pre-specified |
| Analysis type | other[71] |
| Parameter estimate | GMT Ratio |
| Point estimate | 0.97 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.85 |
| upper limit | 1.1 |

Notes:

[71] - Based on a linear model with natural log-transformed OPA titers as response variable, and vaccination group and age
category (2 months of age, ≥3 months of age) as factors.

| **Statistical analysis title** | Serotype 5 |
|---|---|
| Statistical analysis description: | |
| OPA GMT Ratio | |
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 677 |
| Analysis specification | Pre-specified |
| Analysis type | other[72] |
| Parameter estimate | GMT Ratio |
| Point estimate | 0.91 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.8 |
| upper limit | 1.04 |

Notes:

[72] - Based on a linear model with natural log-transformed OPA titers as response variable, and vaccination group and age
category (2 months of age, ≥3 months of age) as factors.

| **Statistical analysis title** | Serotype 6A |
|---|---|
| Statistical analysis description: | |
| OPA GMT Ratio | |
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 677 |
| Analysis specification | Pre-specified |
| Analysis type | other[73] |
| Parameter estimate | GMT Ratio |
| Point estimate | 0.76 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.65 |
| upper limit | 0.89 |

Notes:

[73] - Based on a linear model with natural log-transformed OPA titers as response variable, and vaccination group and age
category (2 months of age, ≥3 months of age) as factors.

| **Statistical analysis title** | Serotype 7F |
|---|---|
| Statistical analysis description: | |
| OPA GMT Ratio | |
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 677 |
| Analysis specification | Pre-specified |
| Analysis type | other[74] |
| Parameter estimate | GMC Ratio |
| Point estimate | 0.81 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.7 |
| upper limit | 0.95 |

Notes:

[74] - Based on a linear model with natural log-transformed OPA titers as response variable, and vaccination group and age
category (2 months of age, ≥3 months of age) as factors.

| **Statistical analysis title** | Serotype 6B |
|---|---|
| Statistical analysis description: | |
| OPA GMT Ratio | |
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 677 |
| Analysis specification | Pre-specified |
| Analysis type | other[75] |
| Parameter estimate | GMC Ratio |
| Point estimate | 0.81 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.69 |
| upper limit | 0.95 |

Notes:

[75] - Based on a linear model with natural log-transformed OPA titers as response variable, and vaccination group and age
category (2 months of age, ≥3 months of age) as factors.

| **Statistical analysis title** | Serotype 9V |
|---|---|
| Statistical analysis description: | |
| OPA GMT Ratio | |
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 677 |
| Analysis specification | Pre-specified |
| Analysis type | other[76] |
| Parameter estimate | GMT Ratio |
| Point estimate | 0.82 |

| | |
|---|---|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.71 |
| upper limit | 0.94 |

Notes:

[76] - Based on a linear model with natural log-transformed OPA titers as response variable, and vaccination group and age
category (2 months of age, ≥3 months of age) as factors.

| **Statistical analysis title** | Serotype 14 |
|---|---|

Statistical analysis description:

OPA GMT Ratio

| | |
|---|---|
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 677 |
| Analysis specification | Pre-specified |
| Analysis type | other[77] |
| Parameter estimate | GMT Ratio |
| Point estimate | 1.15 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.97 |
| upper limit | 1.38 |

Notes:

[77] - Based on a linear model with natural log-transformed OPA titers as response variable, and vaccination group and age
category (2 months of age, ≥3 months of age) as factors.

| **Statistical analysis title** | Serotype 18C |
|---|---|

Statistical analysis description:

OPA GMT Ratio

| | |
|---|---|
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 677 |
| Analysis specification | Pre-specified |
| Analysis type | other[78] |
| Parameter estimate | GMT Ratio |
| Point estimate | 1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.9 |
| upper limit | 1.11 |

Notes:

[78] - Based on a linear model with natural log-transformed OPA titers as response variable, and vaccination group and age
category (2 months of age, ≥3 months of age) as factors.

| **Statistical analysis title** | Serotype 19A |
|---|---|

Statistical analysis description:

OPA GMT Ratio

| | |
|---|---|
| Comparison groups | V114 v PCV13 |

| | |
|---|---|
| Number of subjects included in analysis | 677 |
| Analysis specification | Pre-specified |
| Analysis type | other[79] |
| Parameter estimate | GMT Ratio |
| Point estimate | 0.68 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.61 |
| upper limit | 0.77 |

Notes:

[79] - Based on a linear model with natural log-transformed OPA titers as response variable, and vaccination group and age
category (2 months of age, ≥3 months of age) as factors.

| **Statistical analysis title** | Serotype 19F |
|---|---|

Statistical analysis description:

OPA GMT Ratio

| | |
|---|---|
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 677 |
| Analysis specification | Pre-specified |
| Analysis type | other[80] |
| Parameter estimate | GMT Ratio |
| Point estimate | 0.93 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.84 |
| upper limit | 1.04 |

Notes:

[80] - Based on a linear model with natural log-transformed OPA titers as response variable, and vaccination group and age
category (2 months of age, ≥3 months of age) as factors.

| **Statistical analysis title** | Serotype 23F |
|---|---|

Statistical analysis description:

OPA GMT Ratio

| | |
|---|---|
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 677 |
| Analysis specification | Pre-specified |
| Analysis type | other[81] |
| Parameter estimate | GMT Ratio |
| Point estimate | 0.63 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.53 |
| upper limit | 0.74 |

Notes:

[81] - Based on a linear model with natural log-transformed OPA titers as response variable, and vaccination group and age
category (2 months of age, ≥3 months of age) as factors.

| **Statistical analysis title** | Serotype 22F |
|---|---|

Statistical analysis description:

OPA GMT Ratio

| | |
|---|---|
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 677 |
| Analysis specification | Pre-specified |
| Analysis type | other[82] |
| Parameter estimate | GMT Ratio |
| Point estimate | 560.46 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 474.05 |
| upper limit | 662.63 |

Notes:

[82] - Based on a linear model with natural log-transformed OPA titers as response variable, and vaccination group and age
category (2 months of age, ≥3 months of age) as factors.

| **Statistical analysis title** | Serotype 33F |
|---|---|

Statistical analysis description:

OPA GMT Ratio

| | |
|---|---|
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 677 |
| Analysis specification | Pre-specified |
| Analysis type | other[83] |
| Parameter estimate | GMT Ratio |
| Point estimate | 196.14 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 141.85 |
| upper limit | 271.21 |

Notes:

[83] - Based on a linear model with natural log-transformed OPA titers as response variable, and vaccination group and age
category (2 months of age, ≥3 months of age) as factors.

## Secondary: GMT of Serotype-Specific OPA for Each Serotype in V114 After Dose 4

| End point title | GMT of Serotype-Specific OPA for Each Serotype in V114 After Dose 4 |
|---|---|

End point description:

The anti-PnPs serotype-specific opsonophagocytic activity (OPA) and geometric mean titers (GMTs) of participants administered V114 versus participants administered PCV13 for the 15 serotypes contained in V114 was determined using a multiplexed opsonophagocytic assay. The first 50% of all participants with sufficient serum volume after dose 3 to evaluate OPA responses were analyzed. One participant in the PCV13 group did not receive PCV13 and therefore was not included in the analysis for this end point.

| End point type | Secondary |
|---|---|

End point timeframe:

30 Days after Dose 4, up to a total of 14 months

| End point values | V114 | PCV13 | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 157 | 156 | | |
| Units: Titer | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Serotype 1 (Shared) (n=156, 156) | 453.42 (327.21 to 628.32) | 854.50 (616.64 to 1184.10) | | |
| Serotype 3 (Shared) (n=150, 146) | 1444.00 (1166.36 to 1787.72) | 893.97 (720.25 to 1109.58) | | |
| Serotype 4 (Shared) (n=153, 152) | 4531.52 (3592.99 to 5715.21) | 6264.94 (4957.63 to 7916.97) | | |
| Serotype 5 (Shared) (n=157, 154) | 1853.08 (1439.01 to 2386.30) | 2151.95 (1669.81 to 2773.30) | | |
| Serotype 6A (Shared) (n=152, 152) | 12553.06 (10072.11 to 15645.13) | 17476.24 (13999.28 to 21816.75) | | |
| Serotype 6B (Shared) (n=153, 153) | 9218.64 (7346.96 to 11567.14) | 14041.53 (11171.79 to 17648.42) | | |
| Serotype 7F (Shared) (n=155, 155) | 15451.96 (12500.49 to 19100.31) | 18039.04 (14593.41 to 22298.22) | | |
| Serotype 9V (Shared) (n=152, 154) | 3259.24 (2548.05 to 4168.93) | 5050.89 (3957.89 to 6445.73) | | |
| Serotype 14 (Shared) (n=154, 155) | 8486.72 (6720.27 to 10717.49) | 5719.04 (4521.91 to 7233.08) | | |
| Serotype 18C (Shared) (n=153, 153) | 7027.62 (5704.70 to 8657.32) | 5903.86 (4785.06 to 7284.24) | | |
| Serotype 19A (Shared) (n=155, 156) | 8441.43 (6620.55 to 10763.11) | 10834.58 (8499.57 to 13811.07) | | |
| Serotype 19F (Shared) (n=153, 156) | 4716.70 (3863.66 to 5758.07) | 3829.62 (3138.93 to 4672.28) | | |
| Serotype 23F (Shared) (n=153, 153) | 11319.82 (8635.69 to 14838.22) | 30686.58 (23314.40 to 40389.89) | | |
| Serotype 22F (Unique to V114) (n=156, 144) | 5561.71 (3730.30 to 8292.26) | 35.68 (23.67 to 53.79) | | |
| Serotype 33F (Unique to V114) (n=154, 152) | 19899.34 (14204.44 to 27877.46) | 1183.52 (844.22 to 1659.18) | | |

## Statistical analyses

| Statistical analysis title | Serotype 1 |
|---|---|
| Statistical analysis description: OPA GMT Ratio | |
| Comparison groups | V114 v PCV13 |

| | |
|---|---|
| Number of subjects included in analysis | 313 |
| Analysis specification | Pre-specified |
| Analysis type | other[84] |
| Parameter estimate | GMT Ratio |
| Point estimate | 0.53 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.38 |
| upper limit | 0.75 |

Notes:

[84] - Based on a linear model with natural log-transformed OPA titers as response variable, and vaccination group and age
category (2 months of age, ≥3 months of age) as factors.

| **Statistical analysis title** | Serotype 3 |
|---|---|

Statistical analysis description:

OPA GMT Ratio

| | |
|---|---|
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 313 |
| Analysis specification | Pre-specified |
| Analysis type | other[85] |
| Parameter estimate | GMT Ratio |
| Point estimate | 1.62 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.28 |
| upper limit | 2.03 |

Notes:

[85] - Based on a linear model with natural log-transformed OPA titers as response variable, and vaccination group and age
category (2 months of age, ≥3 months of age) as factors.

| **Statistical analysis title** | Serotype 4 |
|---|---|

Statistical analysis description:

OPA GMT Ratio

| | |
|---|---|
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 313 |
| Analysis specification | Pre-specified |
| Analysis type | other[86] |
| Parameter estimate | GMT Ratio |
| Point estimate | 0.72 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.57 |
| upper limit | 0.93 |

Notes:

[86] - Based on a linear model with natural log-transformed OPA titers as response variable, and vaccination group and age
category (2 months of age, ≥3 months of age) as factors.

| **Statistical analysis title** | Serotype 5 |
|---|---|

| | |
|---|---|
| Statistical analysis description: | |
| OPA GMT Ratio | |
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 313 |
| Analysis specification | Pre-specified |
| Analysis type | other[87] |
| Parameter estimate | GMT Ratio |
| Point estimate | 0.86 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.66 |
| upper limit | 1.13 |

Notes:

[87] - Based on a linear model with natural log-transformed OPA titers as response variable, and vaccination group and age
category (2 months of age, ≥3 months of age) as factors.

| **Statistical analysis title** | Serotype 6A |
|---|---|
| Statistical analysis description: | |
| OPA GMT Ratio | |
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 313 |
| Analysis specification | Pre-specified |
| Analysis type | other[88] |
| Parameter estimate | GMT Ratio |
| Point estimate | 0.72 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.57 |
| upper limit | 0.91 |

Notes:

[88] - Based on a linear model with natural log-transformed OPA titers as response variable, and vaccination group and age
category (2 months of age, ≥3 months of age) as factors.

| **Statistical analysis title** | Serotype 6B |
|---|---|
| Statistical analysis description: | |
| OPA GMT Ratio | |
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 313 |
| Analysis specification | Pre-specified |
| Analysis type | other[89] |
| Parameter estimate | GMT Ratio |
| Point estimate | 0.66 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.52 |
| upper limit | 0.83 |

Notes:

[89] - Based on a linear model with natural log-transformed OPA titers as response variable, and vaccination group and age
category (2 months of age, ≥3 months of age) as factors.

| **Statistical analysis title** | Serotype 7F |
|---|---|
| Statistical analysis description: | |
| OPA GMT Ratio | |
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 313 |
| Analysis specification | Pre-specified |
| Analysis type | other[90] |
| Parameter estimate | GMT Ratio |
| Point estimate | 0.86 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.68 |
| upper limit | 1.07 |

Notes:

[90] - Based on a linear model with natural log-transformed OPA titers as response variable, and vaccination group and age
category (2 months of age, ≥3 months of age) as factors.

| **Statistical analysis title** | Serotype 9V |
|---|---|
| Statistical analysis description: | |
| OPA GMT Ratio | |
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 313 |
| Analysis specification | Pre-specified |
| Analysis type | other[91] |
| Parameter estimate | GMT Ratio |
| Point estimate | 0.65 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.5 |
| upper limit | 0.84 |

Notes:

[91] - Based on a linear model with natural log-transformed OPA titers as response variable, and vaccination group and age
category (2 months of age, ≥3 months of age) as factors.

| **Statistical analysis title** | Serotype 14 |
|---|---|
| Statistical analysis description: | |
| OPA GMT Ratio | |
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 313 |
| Analysis specification | Pre-specified |
| Analysis type | other[92] |
| Parameter estimate | GMT Ratio |
| Point estimate | 1.48 |

| | |
|---|---|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.16 |
| upper limit | 1.9 |

Notes:

[92] - Based on a linear model with natural log-transformed OPA titers as response variable, and vaccination group and age
category (2 months of age, ≥3 months of age) as factors.

| **Statistical analysis title** | Serotype 18C |
|---|---|

Statistical analysis description:

OPA GMT Ratio

| | |
|---|---|
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 313 |
| Analysis specification | Pre-specified |
| Analysis type | other[93] |
| Parameter estimate | GMT Ratio |
| Point estimate | 1.19 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.95 |
| upper limit | 1.48 |

Notes:

[93] - Based on a linear model with natural log-transformed OPA titers as response variable, and vaccination group and age
category (2 months of age, ≥3 months of age) as factors.

| **Statistical analysis title** | Serotype 19A |
|---|---|

Statistical analysis description:

OPA GMT Ratio

| | |
|---|---|
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 313 |
| Analysis specification | Pre-specified |
| Analysis type | other[94] |
| Parameter estimate | GMT Ratio |
| Point estimate | 0.78 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.6 |
| upper limit | 1.01 |

Notes:

[94] - Based on a linear model with natural log-transformed OPA titers as response variable, and vaccination group and age
category (2 months of age, ≥3 months of age) as factors.

| **Statistical analysis title** | Serotype 19F |
|---|---|

Statistical analysis description:

OPA GMT Ratio

| | |
|---|---|
| Comparison groups | V114 v PCV13 |

| | |
|---|---|
| Number of subjects included in analysis | 313 |
| Analysis specification | Pre-specified |
| Analysis type | other[95] |
| Parameter estimate | GMT Ratio |
| Point estimate | 1.23 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1 |
| upper limit | 1.52 |

Notes:

[95] - Based on a linear model with natural log-transformed OPA titers as response variable, and vaccination group and age
category (2 months of age, ≥3 months of age) as factors.

| **Statistical analysis title** | Serotype 23F |
|---|---|

Statistical analysis description:

OPA GMT Ratio

| | |
|---|---|
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 313 |
| Analysis specification | Pre-specified |
| Analysis type | other[96] |
| Parameter estimate | GMT Ratio |
| Point estimate | 0.37 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.28 |
| upper limit | 0.49 |

Notes:

[96] - Based on a linear model with natural log-transformed OPA titers as response variable, and vaccination group and age
category (2 months of age, ≥3 months of age) as factors.

| **Statistical analysis title** | Serotype 22F |
|---|---|

Statistical analysis description:

OPA GMT Ratio

| | |
|---|---|
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 313 |
| Analysis specification | Pre-specified |
| Analysis type | other[97] |
| Parameter estimate | GMT Ratio |
| Point estimate | 155.88 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 101.84 |
| upper limit | 238.59 |

Notes:

[97] - Based on a linear model with natural log-transformed OPA titers as response variable, and vaccination group and age
category (2 months of age, ≥3 months of age) as factors.

| **Statistical analysis title** | Serotype 33F |
|---|---|

| Statistical analysis description: | |
|---|---|
| OPA GMT Ratio | |
| Comparison groups | V114 v PCV13 |
| Number of subjects included in analysis | 313 |
| Analysis specification | Pre-specified |
| Analysis type | other[98] |
| Parameter estimate | GMT Ratio |
| Point estimate | 16.81 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 11.74 |
| upper limit | 24.08 |

Notes:

[98] - Based on a linear model with natural log-transformed OPA titers as response variable, and vaccination group and age
category (2 months of age, ≥3 months of age) as factors.

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Non-serious adverse events: Up to 14 days after each vaccination, up to a total of 13.5 months; Serious adverse events: Approximately 1 month after Dose 4 (Up to 14 months); All-cause mortality: Up to 17 months

Adverse event reporting additional description:

The analysis population for deaths (all-causes) included all randomized participants (N=347, N=347). The analysis population for AEs included all randomized participants who received at least 1 dose of study vaccination. One participant in the PCV13 group did not receive PCV13.

| | |
|---|---|
| Assessment type | Systematic |

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 24.1 |

### 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 | 24 / 347 (6.92%) | 23 / 346 (6.65%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Congenital, familial and genetic disorders | | | |
| Hamartoma | | | |
| subjects affected / exposed | 1 / 347 (0.29%) | 0 / 346 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| Kawasaki's disease | | | |
| subjects affected / exposed | 1 / 347 (0.29%) | 2 / 346 (0.58%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Febrile convulsion | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 347 (0.29%) | 1 / 346 (0.29%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Seizure | | | |
| subjects affected / exposed | 1 / 347 (0.29%) | 0 / 346 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 347 (0.00%) | 1 / 346 (0.29%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Immune system disorders | | | |
| Anaphylactic reaction | | | |
| subjects affected / exposed | 0 / 347 (0.00%) | 1 / 346 (0.29%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Food allergy | | | |
| subjects affected / exposed | 3 / 347 (0.86%) | 1 / 346 (0.29%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Milk allergy | | | |
| subjects affected / exposed | 1 / 347 (0.29%) | 1 / 346 (0.29%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Intussusception | | | |
| subjects affected / exposed | 0 / 347 (0.00%) | 1 / 346 (0.29%) | |
| 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 | | | |
| Asthma | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 347 (0.00%) | 2 / 346 (0.58%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper respiratory tract inflammation | | | |
| subjects affected / exposed | 0 / 347 (0.00%) | 1 / 346 (0.29%) | |
| 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** | | | |
| Compartment syndrome | | | |
| subjects affected / exposed | 0 / 347 (0.00%) | 1 / 346 (0.29%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| **Infections and infestations** | | | |
| Adenovirus infection | | | |
| subjects affected / exposed | 1 / 347 (0.29%) | 0 / 346 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bacterial infection | | | |
| subjects affected / exposed | 1 / 347 (0.29%) | 2 / 346 (0.58%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchiolitis | | | |
| subjects affected / exposed | 0 / 347 (0.00%) | 1 / 346 (0.29%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchitis | | | |
| subjects affected / exposed | 1 / 347 (0.29%) | 2 / 346 (0.58%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| COVID-19 | | | |
| subjects affected / exposed | 1 / 347 (0.29%) | 0 / 346 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Escherichia urinary tract infection | | | |
| subjects affected / exposed | 1 / 347 (0.29%) | 0 / 346 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis norovirus | | | |
| subjects affected / exposed | 1 / 347 (0.29%) | 1 / 346 (0.29%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis viral | | | |
| subjects affected / exposed | 1 / 347 (0.29%) | 0 / 346 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lymphadenitis bacterial | | | |
| subjects affected / exposed | 0 / 347 (0.00%) | 1 / 346 (0.29%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nephritis bacterial | | | |
| subjects affected / exposed | 1 / 347 (0.29%) | 0 / 346 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia | | | |
| subjects affected / exposed | 3 / 347 (0.86%) | 1 / 346 (0.29%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia bacterial | | | |
| subjects affected / exposed | 0 / 347 (0.00%) | 1 / 346 (0.29%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia respiratory syncytial viral | | | |
| subjects affected / exposed | 0 / 347 (0.00%) | 1 / 346 (0.29%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia viral | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 347 (0.00%) | 1 / 346 (0.29%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory syncytial virus bronchiolitis | | | |
| subjects affected / exposed | 0 / 347 (0.00%) | 1 / 346 (0.29%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory syncytial virus bronchitis | | | |
| subjects affected / exposed | 1 / 347 (0.29%) | 2 / 346 (0.58%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory syncytial virus infection | | | |
| subjects affected / exposed | 4 / 347 (1.15%) | 3 / 346 (0.87%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 4 / 347 (1.15%) | 1 / 346 (0.29%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Viral infection | | | |
| subjects affected / exposed | 1 / 347 (0.29%) | 0 / 346 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Viral pharyngitis | | | |
| subjects affected / exposed | 1 / 347 (0.29%) | 0 / 346 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Viral rash | | | |
| subjects affected / exposed | 0 / 347 (0.00%) | 1 / 346 (0.29%) | |
| 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 | 340 / 347 (97.98%) | 340 / 346 (98.27%) | |
| Nervous system disorders | | | |
| Somnolence | | | |
| subjects affected / exposed | 194 / 347 (55.91%) | 190 / 346 (54.91%) | |
| occurrences (all) | 430 | 399 | |
| General disorders and administration site conditions | | | |
| Injection site erythema | | | |
| subjects affected / exposed | 306 / 347 (88.18%) | 309 / 346 (89.31%) | |
| occurrences (all) | 878 | 929 | |
| Injection site induration | | | |
| subjects affected / exposed | 281 / 347 (80.98%) | 281 / 346 (81.21%) | |
| occurrences (all) | 813 | 787 | |
| Injection site pain | | | |
| subjects affected / exposed | 108 / 347 (31.12%) | 83 / 346 (23.99%) | |
| occurrences (all) | 178 | 134 | |
| Injection site swelling | | | |
| subjects affected / exposed | 263 / 347 (75.79%) | 276 / 346 (79.77%) | |
| occurrences (all) | 670 | 688 | |
| Pyrexia | | | |
| subjects affected / exposed | 227 / 347 (65.42%) | 252 / 346 (72.83%) | |
| occurrences (all) | 544 | 610 | |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 35 / 347 (10.09%) | 20 / 346 (5.78%) | |
| occurrences (all) | 43 | 22 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Rhinorrhoea | | | |
| subjects affected / exposed | 10 / 347 (2.88%) | 21 / 346 (6.07%) | |
| occurrences (all) | 12 | 23 | |
| Skin and subcutaneous tissue disorders | | | |
| Eczema infantile | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 18 / 347 (5.19%) | 16 / 346 (4.62%) | |
| occurrences (all) | 19 | 16 | |
| Erythema | | | |
| subjects affected / exposed | 33 / 347 (9.51%) | 31 / 346 (8.96%) | |
| occurrences (all) | 44 | 42 | |
| Rash | | | |
| subjects affected / exposed | 17 / 347 (4.90%) | 18 / 346 (5.20%) | |
| occurrences (all) | 21 | 22 | |
| Skin induration | | | |
| subjects affected / exposed | 23 / 347 (6.63%) | 18 / 346 (5.20%) | |
| occurrences (all) | 29 | 22 | |
| Psychiatric disorders | | | |
| Irritability | | | |
| subjects affected / exposed | 231 / 347 (66.57%) | 210 / 346 (60.69%) | |
| occurrences (all) | 522 | 500 | |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 32 / 347 (9.22%) | 37 / 346 (10.69%) | |
| occurrences (all) | 34 | 39 | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 20 / 347 (5.76%) | 22 / 346 (6.36%) | |
| occurrences (all) | 23 | 29 | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 83 / 347 (23.92%) | 84 / 346 (24.28%) | |
| occurrences (all) | 132 | 117 | |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 25 August 2020 | Amendment 01: Primary reason for amendment was to change the primary objectives for the evaluation of this study. |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported