



Clinical trial results:

A Phase 3, Randomized, Double-blind, Active Comparator-controlled Clinical Study to Evaluate the Safety, Tolerability, and Immunogenicity of V116 in Pneumococcal Vaccine-naïve Adults

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2022-000258-27 |
| Trial protocol | DE SE BE |
| Global end of trial date | 18 May 2023 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 31 May 2024 |
| First version publication date | 31 May 2024 |

Trial information

Trial identification

| | |
|-----------------------|----------|
| Sponsor protocol code | V116-003 |
|-----------------------|----------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT05425732 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

| | |
|--|-------------|
| Analysis stage | Final |
| Date of interim/final analysis | 18 May 2023 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 18 May 2023 |
| Global end of trial reached? | Yes |
| Global end of trial date | 18 May 2023 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

This is a phase 3, randomized, double-blind, active comparator-controlled study of the safety, tolerability, and immunogenicity of V116 compared to PCV20 (pneumococcal 20-valent conjugate vaccine ([Prevnar 20™ / APEXXNAR™]) in pneumococcal vaccine-naïve adults. It is hypothesized that V116 is noninferior to PCV20 for the common serotypes and superior to PCV20 for the unique serotypes as assessed by serotype specific opsonophagocytic activity (OPA) 30 days postvaccination. It is also hypothesized that V116 in participants 18 to 49 years of age immunobridges to V116 in participants 50 to 64 years of age as assessed by serotype specific OPA geometric mean titers (GMTs) 30 days postvaccination for all 21 serotypes in V116. Participants ≥50 years of age will be enrolled in Cohort 1, and participants 18 to 49 years of age will be enrolled in Cohort 2.

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

Background therapy: -

Evidence for comparator: -

| | |
|---|--------------|
| Actual start date of recruitment | 13 July 2022 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------------------|
| Country: Number of subjects enrolled | Australia: 95 |
| Country: Number of subjects enrolled | Belgium: 155 |
| Country: Number of subjects enrolled | Chile: 135 |
| Country: Number of subjects enrolled | Germany: 80 |
| Country: Number of subjects enrolled | New Zealand: 290 |
| Country: Number of subjects enrolled | Puerto Rico: 155 |
| Country: Number of subjects enrolled | Korea, Republic of: 200 |
| Country: Number of subjects enrolled | Sweden: 110 |
| Country: Number of subjects enrolled | Taiwan: 123 |
| Country: Number of subjects enrolled | Türkiye: 56 |
| Country: Number of subjects enrolled | United States: 1264 |
| Worldwide total number of subjects | 2663 |
| EEA total number of subjects | 345 |

Notes:

| Subjects enrolled per age group | |
|---|------|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 1480 |
| From 65 to 84 years | 1156 |
| 85 years and over | 27 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Pneumococcal vaccine-naïve adults ≥ 18 years of age were enrolled in this study. Participants with underlying chronic conditions were eligible if the conditions were assessed to be stable per the investigator's judgment.

Period 1

| | |
|------------------------------|-------------------------|
| Period 1 title | Started/Randomized |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator |

Arms

| | |
|------------------------------|---------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Cohort 1 V116 |

Arm description:

Pneumococcal vaccine-naïve adult participants (≥ 50 years of age) receive a single dose of pneumococcal 21-valent conjugate vaccine (V116) on Day 1.

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

Dosage and administration details:

A single dose of V116 in a 0.5 mL injection solution in prefilled syringe containing 4 μ g of each PnPs antigen (3, 6A, 7F, 8, 9N, 10A, 11A, 12F, 15A, 15C, 16F, 17F, 19A, 20A, 22F, 23A, 23B, 24F, 31, 33F, and 35B) given by intramuscular (IM) injection.

| | |
|------------------|----------------|
| Arm title | Cohort 1 PCV20 |
|------------------|----------------|

Arm description:

Pneumococcal vaccine-naïve adult participants (≥ 50 years of age) receive a single dose of pneumococcal 20-valent conjugate vaccine (PCV20) on Day 1.

| | |
|--|--------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | PCV20 |
| Investigational medicinal product code | |
| Other name | Prevnar 20™ APEXXNAR™ |
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

A single dose of PCV20 in 0.5 mL injection suspension in prefilled syringe containing 2.2 μ g of each PnPs antigen (1, 3, 4, 5, 6A, 7F, 8, 9V, 10A, 11A, 12F, 14, 15B, 18C, 19A, 19F, 22F, 23F, 33F) and 4.4 μ g of PnPs antigen 6B.

| | |
|------------------|---------------|
| Arm title | Cohort 2 V116 |
|------------------|---------------|

Arm description:

Pneumococcal vaccine-naïve adult participants (18 to 49 years of age) receive a single dose of V116 on Day 1.

| | |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

| | |
|--|--|
| Investigational medicinal product name | V116 |
| Investigational medicinal product code | |
| Other name | Pneumococcal 21-valent Conjugate Vaccine |
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

A single dose of V116 in a 0.5 mL injection solution in prefilled syringe containing 4 µg of each PnPs antigen (3, 6A, 7F, 8, 9N, 10A, 11A, 12F, 15A, 15C, 16F, 17F, 19A, 20A, 22F, 23A, 23B, 24F, 31, 33F, and 35B) given by intramuscular (IM) injection.

| | |
|------------------|----------------|
| Arm title | Cohort 2 PCV20 |
|------------------|----------------|

Arm description:

Pneumococcal vaccine-naïve adult participants (18 to 49 years of age) receive a single dose of PCV20 on Day 1.

| | |
|--|--------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | PCV20 |
| Investigational medicinal product code | |
| Other name | Prevnar 20™ APEXXNAR™ |
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

A single dose of PCV20 in 0.5 mL injection suspension in prefilled syringe containing 2.2 µg of each PnPs antigen (1, 3, 4, 5, 6A, 7F, 8, 9V, 10A, 11A, 12F, 14, 15B, 18C, 19A, 19F, 22F, 23F, 33F) and 4.4 µg of PnPs antigen 6B.

| Number of subjects in period 1 | Cohort 1 V116 | Cohort 1 PCV20 | Cohort 2 V116 |
|---|---------------|----------------|---------------|
| Started | 1181 | 1181 | 201 |
| Safety All Cause Mortality (ACM) | 1179 | 1179 | 201 |
| Completed | 1179 | 1177 | 200 |
| Not completed | 2 | 4 | 1 |
| Consent withdrawn by subject | 1 | 1 | 1 |
| Physician decision | - | 1 | - |
| Randomized By Mistake Without Study Treatment | 1 | 2 | - |

| Number of subjects in period 1 | Cohort 2 PCV20 |
|---|----------------|
| Started | 100 |
| Safety All Cause Mortality (ACM) | 100 |
| Completed | 100 |
| Not completed | 0 |
| Consent withdrawn by subject | - |
| Physician decision | - |
| Randomized By Mistake Without Study Treatment | - |

Period 2

| | |
|------------------------------|-------------------------|
| Period 2 title | Vaccinated |
| Is this the baseline period? | Yes ^[1] |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator |

Arms

| | |
|------------------------------|---------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Cohort 1 V116 |

Arm description:

Pneumococcal vaccine-naïve adult participants (≥50 years of age) receive a single dose of pneumococcal 21-valent conjugate vaccine (V116) on Day 1.

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

Dosage and administration details:

A single dose of V116 in a 0.5 mL injection solution in prefilled syringe containing 4 µg of each PnPs antigen (3, 6A, 7F, 8, 9N, 10A, 11A, 12F, 15A, 15C, 16F, 17F, 19A, 20A, 22F, 23A, 23B, 24F, 31, 33F, and 35B) given by intramuscular (IM) injection.

| | |
|------------------|----------------|
| Arm title | Cohort 1 PCV20 |
|------------------|----------------|

Arm description:

Pneumococcal vaccine-naïve adult participants (≥50 years of age) receive a single dose of pneumococcal 20-valent conjugate vaccine (PCV20) on Day 1.

| | |
|--|--------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | PCV20 |
| Investigational medicinal product code | |
| Other name | Prevnar 20™ APEXXNAR™ |
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

A single dose of PCV20 in 0.5 mL injection suspension in prefilled syringe containing 2.2 µg of each PnPs antigen (1, 3, 4, 5, 6A, 7F, 8, 9V, 10A, 11A, 12F, 14, 15B, 18C, 19A, 19F, 22F, 23F, 33F) and 4.4 µg of PnPs antigen 6B.

| | |
|------------------|---------------|
| Arm title | Cohort 2 V116 |
|------------------|---------------|

Arm description:

Pneumococcal vaccine-naïve adult participants (18 to 49 years of age) receive a single dose of V116 on Day 1.

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

Dosage and administration details:

A single dose of V116 in a 0.5 mL injection solution in prefilled syringe containing 4 µg of each PnPs

antigen (3, 6A, 7F, 8, 9N, 10A, 11A, 12F, 15A, 15C, 16F, 17F, 19A, 20A, 22F, 23A, 23B, 24F, 31, 33F, and 35B) given by intramuscular (IM) injection.

| | |
|--|--------------------------|
| Arm title | Cohort 2 PCV20 |
| Arm description: Pneumococcal vaccine-naïve adult participants (18 to 49 years of age) receive a single dose of PCV20 on Day 1. | |
| Arm type | Experimental |
| Investigational medicinal product name | PCV20 |
| Investigational medicinal product code | |
| Other name | Prevnar 20™ APEXXNAR™ |
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

A single dose of PCV20 in 0.5 mL injection suspension in prefilled syringe containing 2.2 µg of each PnPs antigen (1, 3, 4, 5, 6A, 7F, 8, 9V, 10A, 11A, 12F, 14, 15B, 18C, 19A, 19F, 22F, 23F, 33F) and 4.4 µg of PnPs antigen 6B.

Notes:

[1] - Period 1 is not the baseline period. It is expected that period 1 will be the baseline period.

Justification: Instead of Period 1, Period 2, vaccinated, was the baseline period.

| Number of subjects in period 2^[2] | Cohort 1 V116 | Cohort 1 PCV20 | Cohort 2 V116 |
|---|---------------|----------------|---------------|
| Started | 1179 | 1177 | 200 |
| All Participants as Treated (APaT) | 1177 | 1175 | 200 |
| Safety Adverse Event (AE) | 1177 | 1175 | 200 |
| Completed | 1160 | 1152 | 195 |
| Not completed | 19 | 25 | 5 |
| Adverse event, serious fatal | 4 | 2 | - |
| Consent withdrawn by subject | 3 | 7 | - |
| Physician decision | - | 1 | - |
| Randomized to PCV20 then V116 | 2 | - | - |
| Lost to follow-up | 10 | 15 | 5 |

| Number of subjects in period 2^[2] | Cohort 2 PCV20 |
|---|----------------|
| Started | 100 |
| All Participants as Treated (APaT) | 100 |
| Safety Adverse Event (AE) | 100 |
| Completed | 96 |
| Not completed | 4 |
| Adverse event, serious fatal | - |
| Consent withdrawn by subject | 1 |
| Physician decision | - |

| | |
|-------------------------------|---|
| Randomized to PCV20 then V116 | - |
| Lost to follow-up | 3 |

Notes:

[2] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: The number of participants in the baseline period was not the worldwide number enrolled, but rather the number vaccinated.

Baseline characteristics

Reporting groups

| | |
|--|----------------|
| Reporting group title | Cohort 1 V116 |
| Reporting group description: Pneumococcal vaccine-naïve adult participants (≥50 years of age) receive a single dose of pneumococcal 21-valent conjugate vaccine (V116) on Day 1. | |
| Reporting group title | Cohort 1 PCV20 |
| Reporting group description: Pneumococcal vaccine-naïve adult participants (≥50 years of age) receive a single dose of pneumococcal 20-valent conjugate vaccine (PCV20) on Day 1. | |
| Reporting group title | Cohort 2 V116 |
| Reporting group description: Pneumococcal vaccine-naïve adult participants (18 to 49 years of age) receive a single dose of V116 on Day 1. | |
| Reporting group title | Cohort 2 PCV20 |
| Reporting group description: Pneumococcal vaccine-naïve adult participants (18 to 49 years of age) receive a single dose of PCV20 on Day 1. | |

| Reporting group values | Cohort 1 V116 | Cohort 1 PCV20 | Cohort 2 V116 |
|---|---------------|----------------|---------------|
| Number of subjects | 1179 | 1177 | 200 |
| Age Categorical | | | |
| Units: Participants | | | |
| 18 to 49 years | 0 | 0 | 200 |
| 50 to 64 years | 589 | 587 | 0 |
| 65 to 74 years | 464 | 464 | 0 |
| 75 to 84 years | 112 | 113 | 0 |
| ≥85 years | 14 | 13 | 0 |
| Age Continuous | | | |
| Units: Years | | | |
| arithmetic mean | 63.9 | 63.9 | 35.2 |
| standard deviation | ± 8.3 | ± 8.3 | ± 9.0 |
| Sex: Female, Male | | | |
| Units: | | | |
| Female | 687 | 670 | 137 |
| Male | 492 | 507 | 63 |
| Race (NIH/OMB) | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 4 | 4 | 0 |
| Asian | 148 | 168 | 38 |
| Native Hawaiian or Other Pacific Islander | 17 | 16 | 1 |
| Black or African American | 116 | 115 | 13 |
| White | 867 | 844 | 139 |
| More than one race | 26 | 30 | 9 |
| Unknown or Not Reported | 1 | 0 | 0 |
| Ethnicity (NIH/OMB) | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 259 | 242 | 58 |

| | | | |
|-------------------------|-----|-----|-----|
| Not Hispanic or Latino | 909 | 922 | 141 |
| Unknown or Not Reported | 11 | 13 | 1 |

| Reporting group values | Cohort 2 PCV20 | Total | |
|---|----------------|-------|--|
| Number of subjects | 100 | 2656 | |
| Age Categorical Units: Participants | | | |
| 18 to 49 years | 100 | 300 | |
| 50 to 64 years | 0 | 1176 | |
| 65 to 74 years | 0 | 928 | |
| 75 to 84 years | 0 | 225 | |
| ≥85 years | 0 | 27 | |
| Age Continuous Units: Years | | | |
| arithmetic mean | 34.6 | | |
| standard deviation | ± 8.7 | - | |
| Sex: Female, Male Units: | | | |
| Female | 64 | 1558 | |
| Male | 36 | 1098 | |
| Race (NIH/OMB) Units: Subjects | | | |
| American Indian or Alaska Native | 1 | 9 | |
| Asian | 15 | 369 | |
| Native Hawaiian or Other Pacific Islander | 2 | 36 | |
| Black or African American | 14 | 258 | |
| White | 62 | 1912 | |
| More than one race | 6 | 71 | |
| Unknown or Not Reported | 0 | 1 | |
| Ethnicity (NIH/OMB) Units: Subjects | | | |
| Hispanic or Latino | 24 | 583 | |
| Not Hispanic or Latino | 76 | 2048 | |
| Unknown or Not Reported | 0 | 25 | |

End points

End points reporting groups

| | |
|--|-------------------------|
| Reporting group title | Cohort 1 V116 |
| Reporting group description: Pneumococcal vaccine-naïve adult participants (≥50 years of age) receive a single dose of pneumococcal 21-valent conjugate vaccine (V116) on Day 1. | |
| Reporting group title | Cohort 1 PCV20 |
| Reporting group description: Pneumococcal vaccine-naïve adult participants (≥50 years of age) receive a single dose of pneumococcal 20-valent conjugate vaccine (PCV20) on Day 1. | |
| Reporting group title | Cohort 2 V116 |
| Reporting group description: Pneumococcal vaccine-naïve adult participants (18 to 49 years of age) receive a single dose of V116 on Day 1. | |
| Reporting group title | Cohort 2 PCV20 |
| Reporting group description: Pneumococcal vaccine-naïve adult participants (18 to 49 years of age) receive a single dose of PCV20 on Day 1. | |
| Reporting group title | Cohort 1 V116 |
| Reporting group description: Pneumococcal vaccine-naïve adult participants (≥50 years of age) receive a single dose of pneumococcal 21-valent conjugate vaccine (V116) on Day 1. | |
| Reporting group title | Cohort 1 PCV20 |
| Reporting group description: Pneumococcal vaccine-naïve adult participants (≥50 years of age) receive a single dose of pneumococcal 20-valent conjugate vaccine (PCV20) on Day 1. | |
| Reporting group title | Cohort 2 V116 |
| Reporting group description: Pneumococcal vaccine-naïve adult participants (18 to 49 years of age) receive a single dose of V116 on Day 1. | |
| Reporting group title | Cohort 2 PCV20 |
| Reporting group description: Pneumococcal vaccine-naïve adult participants (18 to 49 years of age) receive a single dose of PCV20 on Day 1. | |
| Subject analysis set title | V116 18 to 49 years old |
| Subject analysis set type | Per protocol |
| Subject analysis set description: Pneumococcal vaccine-naïve adult participants 18 to 49 years of age receive a single dose of V116 on Day 1. | |
| Subject analysis set title | V116 50 to 64 years old |
| Subject analysis set type | Per protocol |
| Subject analysis set description: Pneumococcal vaccine-naïve adult participants 50 to 64 years of age receive a single dose of V116 on Day 1. | |
| Subject analysis set title | V116 18 to 49 years old |
| Subject analysis set type | Per protocol |
| Subject analysis set description: Pneumococcal vaccine-naïve adult participants in Cohort 2 (18 to 49 years of age) receive a single dose of V116 on Day 1. | |
| Subject analysis set title | V116 50 to 64 years old |
| Subject analysis set type | Per protocol |
| Subject analysis set description: Pneumococcal vaccine-naïve adult participants in Cohort 1 50 to 64 years of age receive a single dose of | |

Primary: Percentage of participants with solicited injection-site adverse events (AEs)

| | |
|-----------------|---|
| End point title | Percentage of participants with solicited injection-site adverse events (AEs) |
|-----------------|---|

End point description:

An AE is any untoward medical occurrence in a clinical study participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention. Solicited injection-site AEs consist of the following: pain/tenderness, redness/erythema, and swelling. The population analyzed was all participants as treated consisting of randomized participants who were included in the group corresponding to the vaccine actually received.

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

End point timeframe:

Up to 5 days post-vaccination

| End point values | Cohort 1 V116 | Cohort 1 PCV20 | Cohort 2 V116 | Cohort 2 PCV20 |
|-----------------------------------|-----------------|-----------------|-----------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 1177 | 1175 | 200 | 100 |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| Injection site erythema | 5.4 | 6.3 | 15.5 | 13.0 |
| Injection site pain | 39.4 | 51.7 | 71.5 | 74.0 |
| Injection site swelling | 6.0 | 8.3 | 14.0 | 14.0 |

Statistical analyses

| | |
|-----------------------------------|-------------------------|
| Statistical analysis title | Injection site erythema |
|-----------------------------------|-------------------------|

Statistical analysis description:

Estimated difference in percent

| | |
|---|--------------------------------|
| Comparison groups | Cohort 1 V116 v Cohort 1 PCV20 |
| Number of subjects included in analysis | 2352 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Difference in Percent |
| Point estimate | -0.9 |
| Confidence interval | |
| level | Other: 96 % |
| sides | 2-sided |
| lower limit | -2.8 |
| upper limit | 1.1 |

| | |
|-----------------------------------|---------------------|
| Statistical analysis title | Injection site pain |
|-----------------------------------|---------------------|

| | |
|---|--------------------------------|
| Statistical analysis description: | |
| Estimated difference in percent | |
| Comparison groups | Cohort 1 V116 v Cohort 1 PCV20 |
| Number of subjects included in analysis | 2352 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Difference in Percent |
| Point estimate | -12.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -16.2 |
| upper limit | -8.2 |

| | |
|---|--------------------------------|
| Statistical analysis title | Injection site swelling |
| Statistical analysis description: | |
| Estimated difference in percent | |
| Comparison groups | Cohort 2 V116 v Cohort 2 PCV20 |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Difference in Percent |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -9.2 |
| upper limit | 7.9 |

| | |
|---|--------------------------------|
| Statistical analysis title | Injection site erythema: |
| Statistical analysis description: | |
| Estimated difference in percent | |
| Comparison groups | Cohort 2 V116 v Cohort 2 PCV20 |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Difference in Percent |
| Point estimate | 2.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -6.6 |
| upper limit | 10.3 |

| | |
|---|--------------------------------|
| Statistical analysis title | Injection site pain |
| Statistical analysis description: | |
| Estimated difference in percent | |
| Comparison groups | Cohort 2 V116 v Cohort 2 PCV20 |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Difference in Percent |
| Point estimate | -2.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -12.7 |
| upper limit | 8.6 |

| | |
|---|--------------------------------|
| Statistical analysis title | Injection site swelling |
| Statistical analysis description: | |
| Estimated difference in percent | |
| Comparison groups | Cohort 1 V116 v Cohort 1 PCV20 |
| Number of subjects included in analysis | 2352 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Difference in Percent |
| Point estimate | -2.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -4.4 |
| upper limit | -0.2 |

Primary: Percentage of participants with solicited systemic AEs

| | |
|--|--|
| End point title | Percentage of participants with solicited systemic AEs |
| End point description: | |
| <p>An AE is any untoward medical occurrence in a clinical study participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention. Solicited systemic AEs consist of the following: fatigue (tiredness), headache, myalgia (muscle aches), and pyrexia (maximum temperature ≥ 100.4 °F/38.0 °C). The population analyzed was all participants as treated consisting of randomized participants who were included in the group corresponding to the vaccine actually received.</p> | |
| End point type | Primary |
| End point timeframe: | |
| Up to 5 days post-vaccination | |

| End point values | Cohort 1 V116 | Cohort 1 PCV20 | Cohort 2 V116 | Cohort 2 PCV20 |
|-----------------------------------|-----------------|-----------------|-----------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 1177 | 1175 | 200 | 100 |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| Fatigue | 20.1 | 19.6 | 40.5 | 34.0 |
| Headache | 11.5 | 12.9 | 29.5 | 24.0 |
| Myalgia | 5.9 | 6.7 | 16.5 | 14.0 |
| Pyrexia | 1.3 | 1.3 | 3.5 | 1.0 |

Statistical analyses

| | |
|---|--------------------------------|
| Statistical analysis title | Fatigue |
| Statistical analysis description: | |
| Estimated difference in percent | |
| Comparison groups | Cohort 1 V116 v Cohort 1 PCV20 |
| Number of subjects included in analysis | 2352 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Difference in Percent |
| Point estimate | 0.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.7 |
| upper limit | 3.8 |

| | |
|---|--------------------------------|
| Statistical analysis title | Headache |
| Statistical analysis description: | |
| Estimated difference in percent | |
| Comparison groups | Cohort 1 V116 v Cohort 1 PCV20 |
| Number of subjects included in analysis | 2352 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Difference in Percent |
| Point estimate | -1.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -4.1 |
| upper limit | 1.2 |

| | |
|-----------------------------------|---------|
| Statistical analysis title | Fatigue |
|-----------------------------------|---------|

| | |
|---|--------------------------------|
| Statistical analysis description: | |
| Estimated difference in percent | |
| Comparison groups | Cohort 2 V116 v Cohort 2 PCV20 |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Difference in Percent |
| Point estimate | 6.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -5.3 |
| upper limit | 17.6 |

| | |
|---|--------------------------------|
| Statistical analysis title | Headache |
| Statistical analysis description: | |
| Estimated difference in percent | |
| Comparison groups | Cohort 2 V116 v Cohort 2 PCV20 |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Difference in Percent |
| Point estimate | 5.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -5.5 |
| upper limit | 15.5 |

| | |
|---|--------------------------------|
| Statistical analysis title | Myalgia |
| Statistical analysis description: | |
| Estimated difference in percent | |
| Comparison groups | Cohort 2 V116 v Cohort 2 PCV20 |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Difference in Percent |
| Point estimate | 2.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -6.8 |
| upper limit | 10.6 |

| | |
|---|--------------------------------|
| Statistical analysis title | Pyrexia |
| Statistical analysis description: | |
| Estimated difference in percent | |
| Comparison groups | Cohort 2 V116 v Cohort 2 PCV20 |
| Number of subjects included in analysis | 300 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Difference in Percent |
| Point estimate | 2.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.2 |
| upper limit | 6.2 |

| | |
|---|--------------------------------|
| Statistical analysis title | Myalgia: |
| Statistical analysis description: | |
| Estimated difference in percent | |
| Comparison groups | Cohort 1 V116 v Cohort 1 PCV20 |
| Number of subjects included in analysis | 2352 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Difference in Percent |
| Point estimate | -0.8 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.8 |
| upper limit | 1.2 |

| | |
|---|--------------------------------|
| Statistical analysis title | Pyrexia |
| Statistical analysis description: | |
| Estimated difference in percent | |
| Comparison groups | Cohort 1 V116 v Cohort 1 PCV20 |
| Number of subjects included in analysis | 2352 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Difference in Percent |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1 |
| upper limit | 1 |

Primary: Percentage of participants with vaccine-related serious AE (SAE)

| | |
|-----------------|---|
| End point title | Percentage of participants with vaccine-related serious AE (SAE) ^[1] |
|-----------------|---|

End point description:

A vaccine-related SAE is any untoward medical consequence that results in death, is life-threatening, requires inpatient hospitalization or prolongs existing hospitalization, results in persistent or significant disability/incapacity, is a congenital anomaly/birth defect, or is an other important medical event, which is determined by the investigator to be related to the vaccine. The population analyzed was all participants as treated consisting of randomized participants who were included in the group corresponding to the vaccine actually received.

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

End point timeframe:

Up to 194 days post-vaccination

Notes:

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

Justification: No statistical comparison was specified because the results were zero.

| End point values | Cohort 1 V116 | Cohort 1 PCV20 | Cohort 2 V116 | Cohort 2 PCV20 |
|-----------------------------------|-----------------|-----------------|-----------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 1177 | 1175 | 200 | 100 |
| Units: Percentage of participants | | | | |
| number (not applicable) | 0.0 | 0.0 | 0.0 | 0.0 |

Statistical analyses

No statistical analyses for this end point

Primary: Serotype specific opsonophagocytic (OPA) geometric mean titers (GMTs) in Cohort 1 only, for the pneumococcal serotypes contained in V116 and PCV20

| | |
|-----------------|--|
| End point title | Serotype specific opsonophagocytic (OPA) geometric mean titers (GMTs) in Cohort 1 only, for the pneumococcal serotypes contained in V116 and PCV20 |
|-----------------|--|

End point description:

The serotype specific OPA GMTs for the pneumococcal serotypes in cohort 1 only were determined using the multiplex opsonophagocytic assay (MOPA). GMT values were estimated from a constrained longitudinal data analysis; (cLDA) model. The 10 common pneumococcal serotypes in both V116 and PCV20 were as follows: 3, 6A, 7F, 8, 10A, 11A, 12F, 19A, 22F, and 33F. The 11 unique pneumococcal serotypes in V116 were as follows: 9N, 15A, 15C, 16F, 17F, 20A, 23A, 23B, 24F, 31, and 35B. 99999 means per protocol, within group CIs, or any other measures of dispersion, were not determined. The population analyzed was all randomized participants from cohort 1 only, without deviations from the protocol that may substantially affect immunogenicity. Deviations include, but are not limited to the following: missing serology results; and blood draw out of window.

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

End point timeframe:

Day 30 post-vaccination

| End point values | Cohort 1 V116 | Cohort 1 PCV20 | Cohort 2 V116 | Cohort 2 PCV20 |
|--|----------------------|----------------------|------------------|------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 1179 | 1177 | 0 ^[2] | 0 ^[3] |
| Units: Titer | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Serotype 3 | 274.0 (0 to 99999) | 176.7 (0 to 99999) | (to) | (to) |
| Serotype 6A | 2302.0 (0 to 99999) | 2972.5 (0 to 99999) | (to) | (to) |
| Serotype 7F | 3637.4 (0 to 99999) | 3429.9 (0 to 99999) | (to) | (to) |
| Serotype 8 | 2501.3 (90 to 99999) | 1811.1 (0 to 99999) | (to) | (to) |
| Serotype 10A | 3893.4 (0 to 99999) | 4678.0 (0 to 99999) | (to) | (to) |
| Serotype 11A | 3232.6 (0 to 99999) | 2092.8 (0 to 99999) | (to) | (to) |
| Serotype 12F | 2641.2 (0 to 99999) | 2499.6 (0 to 99999) | (to) | (to) |
| Serotype 19A | 2136.1 (0 to 99999) | 2817.8 (0 to 99999) | (to) | (to) |
| Serotype 22F | 3874.5 (0 to 99999) | 4770.1 (0 to 99999) | (to) | (to) |
| Serotype 33F | 13558.9 (0 to 99999) | 11742.1 (0 to 99999) | (to) | (to) |
| Serotype 9N | 7470.7 (0 to 99999) | 1640.4 (0 to 99999) | (to) | (to) |
| Serotype 15A | 5237.2 (0 to 99999) | 1589.0 (0 to 99999) | (to) | (to) |
| Serotype 15C | 4216.2 (0 to 99999) | 2072.3 (0 to 99999) | (to) | (to) |
| Serotype 16F | 4868.2 (0 to 99999) | 846.3 (0 to 99999) | (to) | (to) |
| Serotype 17F | 7764.9 (0 to 99999) | 460.4 (0 to 99999) | (to) | (to) |
| Serotype 20A | 6099.2 (0 to 99999) | 631.1 (0 to 99999) | (to) | (to) |
| Serotype 23A | 3737.2 (0 to 99999) | 461.5 (0 to 99999) | (to) | (to) |
| Serotype 23B | 1082.5 (0 to 99999) | 107.3 (0 to 99999) | (to) | (to) |
| Serotype 24F | 2728.6 (0 to 99999) | 70.5 (0 to 99999) | (to) | (to) |
| Serotype 31 | 3132.5 (0 to 99999) | 144.4 (0 to 99999) | (to) | (to) |
| Serotype 35B | 8527.8 (0 to 99999) | 1383.0 (0 to 99999) | (to) | (to) |

Notes:

[2] - Per protocol, Cohort 2 were not analyzed in this endpoint.

[3] - Per protocol, Cohort 2 were not analyzed in this endpoint.

Statistical analyses

| | |
|---|--------------------------------|
| Statistical analysis title | Serotype 3 |
| Statistical analysis description: V116/PCV20 GMT Ratio | |
| Comparison groups | Cohort 1 V116 v Cohort 1 PCV20 |

| | |
|---|------------------------|
| Number of subjects included in analysis | 2356 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.001 ^[4] |
| Method | cLDA model |
| Parameter estimate | GMT Ratio |
| Point estimate | 1.55 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.4 |
| upper limit | 1.72 |

Notes:

[4] - 1-sided

| | |
|---|--------------------------------|
| Statistical analysis title | Serotype 6A |
| Statistical analysis description: V116/PCV20 GMT Ratio | |
| Comparison groups | Cohort 1 V116 v Cohort 1 PCV20 |
| Number of subjects included in analysis | 2356 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.001 |
| Method | cLDA model |
| Parameter estimate | GMT Ratio |
| Point estimate | 0.77 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.68 |
| upper limit | 0.88 |

| | |
|---|--------------------------------|
| Statistical analysis title | Serotype 9N |
| Statistical analysis description: V116/PCV20 GMT Ratio | |
| Comparison groups | Cohort 1 V116 v Cohort 1 PCV20 |
| Number of subjects included in analysis | 2356 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.001 |
| Method | cLDA model |
| Parameter estimate | GMT Ratio |
| Point estimate | 4.55 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 4.12 |
| upper limit | 5.04 |

| | |
|---|--------------------------------|
| Statistical analysis title | Serotype 33F |
| Statistical analysis description: V116/PCV20 GMT Ratio | |
| Comparison groups | Cohort 1 V116 v Cohort 1 PCV20 |
| Number of subjects included in analysis | 2356 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.001 |
| Method | cLDA model |
| Parameter estimate | GMT Ratio |
| Point estimate | 1.15 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.01 |
| upper limit | 1.32 |

| | |
|---|--------------------------------|
| Statistical analysis title | Serotype 22F |
| Statistical analysis description: V116/PCV20 GMT Ratio | |
| Comparison groups | Cohort 1 V116 v Cohort 1 PCV20 |
| Number of subjects included in analysis | 2356 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.001 |
| Method | cLDA model |
| Parameter estimate | GMT Ratio |
| Point estimate | 0.81 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.72 |
| upper limit | 0.92 |

| | |
|---|--------------------------------|
| Statistical analysis title | Serotype 19A |
| Statistical analysis description: V116/PCV20 GMT Ratio | |
| Comparison groups | Cohort 1 V116 v Cohort 1 PCV20 |

| | |
|---|---------------|
| Number of subjects included in analysis | 2356 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.001 |
| Method | cLDA model |
| Parameter estimate | GMT Ratio |
| Point estimate | 0.76 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.69 |
| upper limit | 0.84 |

| | |
|---|--------------------------------|
| Statistical analysis title | Serotype 12F |
| Statistical analysis description: V116/PCV20 GMT Ratio | |
| Comparison groups | Cohort 1 V116 v Cohort 1 PCV20 |
| Number of subjects included in analysis | 2356 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.001 |
| Method | cLDA model |
| Parameter estimate | GMT Ratio |
| Point estimate | 1.06 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.92 |
| upper limit | 1.21 |

| | |
|---|--------------------------------|
| Statistical analysis title | Serotype 11A |
| Statistical analysis description: V116/PCV20 GMT Ratio | |
| Comparison groups | Cohort 1 V116 v Cohort 1 PCV20 |
| Number of subjects included in analysis | 2356 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.001 |
| Method | cLDA model |
| Parameter estimate | GMT Ratio |
| Point estimate | 1.54 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.39 |
| upper limit | 1.72 |

| | |
|---|--------------------------------|
| Statistical analysis title | Serotype 10A |
| Statistical analysis description: V116/PCV20 GMT Ratio | |
| Comparison groups | Cohort 1 V116 v Cohort 1 PCV20 |
| Number of subjects included in analysis | 2356 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.001 |
| Method | cLDA model |
| Parameter estimate | GMT Ratio |
| Point estimate | 0.83 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.75 |
| upper limit | 0.93 |

| | |
|---|--------------------------------|
| Statistical analysis title | Serotype 8 |
| Statistical analysis description: V116/PCV20 GMT Ratio | |
| Comparison groups | Cohort 1 V116 v Cohort 1 PCV20 |
| Number of subjects included in analysis | 2356 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.001 |
| Method | cLDA model |
| Parameter estimate | GMT Ratio |
| Point estimate | 1.38 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.25 |
| upper limit | 1.53 |

| | |
|---|--------------------------------|
| Statistical analysis title | Serotype 7 |
| Statistical analysis description: V116/PCV20 GMT Ratio | |
| Comparison groups | Cohort 1 V116 v Cohort 1 PCV20 |

| | |
|---|---------------|
| Number of subjects included in analysis | 2356 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.001 |
| Method | cLDA model |
| Parameter estimate | GMT Ratio |
| Point estimate | 1.06 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.95 |
| upper limit | 1.18 |

| | |
|---|--------------------------------|
| Statistical analysis title | Serotype 31 |
| Statistical analysis description: V116/PCV20 GMT Ratio | |
| Comparison groups | Cohort 1 V116 v Cohort 1 PCV20 |
| Number of subjects included in analysis | 2356 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.001 |
| Method | cLDA model |
| Parameter estimate | GMT Ratio |
| Point estimate | 21.69 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 18.68 |
| upper limit | 25.18 |

| | |
|---|--------------------------------|
| Statistical analysis title | Serotype 24F |
| Statistical analysis description: V116/PCV20 GMT Ratio | |
| Comparison groups | Cohort 1 V116 v Cohort 1 PCV20 |
| Number of subjects included in analysis | 2356 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.001 |
| Method | cLDA model |
| Parameter estimate | GMT Ratio |
| Point estimate | 38.71 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 33.87 |
| upper limit | 44.25 |

| | |
|---|--------------------------------|
| Statistical analysis title | Serotype 23B |
| Statistical analysis description: V116/PCV20 GMT Ratio | |
| Comparison groups | Cohort 1 V116 v Cohort 1 PCV20 |
| Number of subjects included in analysis | 2356 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.001 |
| Method | cLDA model |
| Parameter estimate | GMT Ratio |
| Point estimate | 10.09 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 8.48 |
| upper limit | 12 |

| | |
|---|--------------------------------|
| Statistical analysis title | Serotype 23A |
| Statistical analysis description: V116/PCV20 GMT Ratio | |
| Comparison groups | Cohort 1 V116 v Cohort 1 PCV20 |
| Number of subjects included in analysis | 2356 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.001 |
| Method | cLDA model |
| Parameter estimate | GMT Ratio |
| Point estimate | 8.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 6.86 |
| upper limit | 9.55 |

| | |
|---|--------------------------------|
| Statistical analysis title | Serotype 35B |
| Statistical analysis description: V116/PCV20 GMT Ratio | |
| Comparison groups | Cohort 1 V116 v Cohort 1 PCV20 |

| | |
|---|---------------|
| Number of subjects included in analysis | 2356 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.001 |
| Method | cLDA model |
| Parameter estimate | GMT Ratio |
| Point estimate | 6.17 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 5.59 |
| upper limit | 6.8 |

| | |
|---|--------------------------------|
| Statistical analysis title | Serotype 17F |
| Statistical analysis description: V116/PCV20 GMT Ratio | |
| Comparison groups | Cohort 1 V116 v Cohort 1 PCV20 |
| Number of subjects included in analysis | 2356 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.001 |
| Method | cLDA model |
| Parameter estimate | GMT Ratio |
| Point estimate | 16.86 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 14.9 |
| upper limit | 19.09 |

| | |
|---|--------------------------------|
| Statistical analysis title | Serotype 16F |
| Statistical analysis description: V116/PCV20 GMT Ratio | |
| Comparison groups | Cohort 1 V116 v Cohort 1 PCV20 |
| Number of subjects included in analysis | 2356 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.001 |
| Method | cLDA model |
| Parameter estimate | GMT Ratio |
| Point estimate | 5.75 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 5.16 |
| upper limit | 6.41 |

| | |
|---|--------------------------------|
| Statistical analysis title | Serotype 15C |
| Statistical analysis description: V116/PCV20 GMT Ratio | |
| Comparison groups | Cohort 1 V116 v Cohort 1 PCV20 |
| Number of subjects included in analysis | 2356 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.001 |
| Method | cLDA model |
| Parameter estimate | GMT Ratio |
| Point estimate | 2.03 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.77 |
| upper limit | 2.34 |

| | |
|---|--------------------------------|
| Statistical analysis title | Serotype 15A |
| Statistical analysis description: V116/PCV20 GMT Ratio | |
| Comparison groups | Cohort 1 V116 v Cohort 1 PCV20 |
| Number of subjects included in analysis | 2356 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.001 |
| Method | cLDA model |
| Parameter estimate | GMT Ratio |
| Point estimate | 3.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 2.91 |
| upper limit | 3.74 |

| | |
|---|--------------------------------|
| Statistical analysis title | Serotype 20A |
| Statistical analysis description: V116/PCV20 GMT Ratio | |
| Comparison groups | Cohort 1 V116 v Cohort 1 PCV20 |

| | |
|---|---------------|
| Number of subjects included in analysis | 2356 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.001 |
| Method | cLDA model |
| Parameter estimate | GMT Ratio |
| Point estimate | 9.66 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 8.66 |
| upper limit | 10.79 |

Primary: Percentage of participants with ≥ 4 -fold change from baseline in serotype specific OPA responses in Cohort 1 only for the 11 unique pneumococcal serotypes contained in V116.

| | |
|-----------------|---|
| End point title | Percentage of participants with ≥ 4 -fold change from baseline in serotype specific OPA responses in Cohort 1 only for the 11 unique pneumococcal serotypes contained in V116. |
|-----------------|---|

End point description:

The percentage of participants with ≥ 4 -fold rise from baseline in serotype specific OPAs for the 11 unique pneumococcal serotypes contained in V116. Per protocol, within group CIs or any other measures of dispersion were not planned or determined. The 11 unique pneumococcal serotypes in V116 were as follows: 9N, 15A, 15C, 16F, 17F, 20A, 23A, 23B, 24F, 31, and 35B. 99999 means per protocol, within group CIs, or any other measures of dispersion, were not determined. The population analyzed was all randomized participants from cohort 1 only, without deviations from the protocol that may substantially affect immunogenicity. Deviations include, but are not limited to the following: missing serology results; and blood draw out of window

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

End point timeframe:

Baseline and Day 30 post-vaccination

| End point values | Cohort 1 V116 | Cohort 1 PCV20 | Cohort 2 V116 | Cohort 2 PCV20 |
|-----------------------------------|-------------------|-------------------|------------------|------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 1179 | 1177 | 0 ^[5] | 0 ^[6] |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| Serotype 9N | 64.7 (0 to 99999) | 19.9 (0 to 99999) | (to) | (to) |
| Serotype 15A | 66.7 (0 to 99999) | 35.8 (0 to 99999) | (to) | (to) |
| Serotype 15C | 83.4 (0 to 99999) | 74.2 (0 to 99999) | (to) | (to) |
| Serotype 16F | 71.9 (0 to 99999) | 20.8 (0 to 99999) | (to) | (to) |
| Serotype 17F | 75.8 (0 to 99999) | 9.5 (0 to 99999) | (to) | (to) |
| Serotype 20A | 67.3 (0 to 99999) | 9.6 (0 to 99999) | (to) | (to) |
| Serotype 23A | 78.9 (0 to 99999) | 36.8 (0 to 99999) | (to) | (to) |

| | | | | |
|--------------|-------------------|-------------------|--------|--------|
| Serotype 23B | 85.5 (0 to 99999) | 49.6 (0 to 99999) | (to) | (to) |
| Serotype 24F | 80.5 (0 to 99999) | 6.3 (0 to 99999) | (to) | (to) |
| Serotype 31 | 76.5 (0 to 99999) | 17.9 (0 to 99999) | (to) | (to) |
| Serotype 35B | 60.0 (0 to 99999) | 6.8 (0 to 99999) | (to) | (to) |

Notes:

[5] - Per protocol, Cohort 2 were not analyzed in this endpoint.

[6] - Per protocol, Cohort 2 were not analyzed in this endpoint.

Statistical analyses

| Statistical analysis title | Serotype 15A |
|---|---------------------------------|
| Statistical analysis description: V116-PCV20 Percentage Difference | |
| Comparison groups | Cohort 1 V116 v Cohort 1 PCV20 |
| Number of subjects included in analysis | 2356 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.001 ^[7] |
| Method | Stratified Miettinen & Nurminen |
| Parameter estimate | Percent Difference |
| Point estimate | 30.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 25.8 |
| upper limit | 35.8 |

Notes:

[7] - 1-sided

| Statistical analysis title | Serotype 9N |
|---|---------------------------------|
| Statistical analysis description: V116-PCV20 Percentage Difference | |
| Comparison groups | Cohort 1 V116 v Cohort 1 PCV20 |
| Number of subjects included in analysis | 2356 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.001 ^[8] |
| Method | Stratified Miettinen & Nurminen |
| Parameter estimate | Percent Difference |
| Point estimate | 44.7 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 40.7 |
| upper limit | 48.6 |

Notes:

[8] - 1-sided

| | |
|---|---------------------------------|
| Statistical analysis title | Serotype 16F |
| Statistical analysis description: V116-PCV20 Percentage Difference | |
| Comparison groups | Cohort 1 V116 v Cohort 1 PCV20 |
| Number of subjects included in analysis | 2356 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.001 ^[9] |
| Method | Stratified Miettinen & Nurminen |
| Parameter estimate | Percent Difference |
| Point estimate | 51.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 47.1 |
| upper limit | 54.9 |

Notes:

[9] - 1-sided

| | |
|---|---------------------------------|
| Statistical analysis title | Serotype 15C |
| Statistical analysis description: V116-PCV20 Percentage Difference | |
| Comparison groups | Cohort 1 V116 v Cohort 1 PCV20 |
| Number of subjects included in analysis | 2356 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.001 ^[10] |
| Method | Stratified Miettinen & Nurminen |
| Parameter estimate | Percent Difference |
| Point estimate | 9.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 5.6 |
| upper limit | 12.9 |

Notes:

[10] - 1-sided

| | |
|---|---------------------------------|
| Statistical analysis title | Serotype24F |
| Statistical analysis description: V116-PCV20 Percentage Difference | |
| Comparison groups | Cohort 1 V116 v Cohort 1 PCV20 |
| Number of subjects included in analysis | 2356 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.001 ^[11] |
| Method | Stratified Miettinen & Nurminen |
| Parameter estimate | Percent Difference |
| Point estimate | 74.2 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 71.1 |
| upper limit | 77.1 |

Notes:

[11] - 1-sided

| | |
|---|---------------------------------|
| Statistical analysis title | Serotype 31 |
| Statistical analysis description: V116-PCV20 Percentage Difference | |
| Comparison groups | Cohort 1 V116 v Cohort 1 PCV20 |
| Number of subjects included in analysis | 2356 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.001 ^[12] |
| Method | Stratified Miettinen & Nurminen |
| Parameter estimate | Percent Difference |
| Point estimate | 58.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 54.8 |
| upper limit | 62.1 |

Notes:

[12] - 1-sided

| | |
|---|---------------------------------|
| Statistical analysis title | Serotype 23B |
| Statistical analysis description: V116-PCV20 Percentage Difference | |
| Comparison groups | Cohort 1 V116 v Cohort 1 PCV20 |
| Number of subjects included in analysis | 2356 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.001 ^[13] |
| Method | Stratified Miettinen & Nurminen |
| Parameter estimate | Percent Difference |
| Point estimate | 35.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 32.1 |
| upper limit | 39.6 |

Notes:

[13] - 1-sided

| | |
|---|--------------------------------|
| Statistical analysis title | Serotype 23A |
| Statistical analysis description: V116-PCV20 Percentage Difference | |
| Comparison groups | Cohort 1 V116 v Cohort 1 PCV20 |

| | |
|---|---------------------------------|
| Number of subjects included in analysis | 2356 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.001 ^[14] |
| Method | Stratified Miettinen & Nurminen |
| Parameter estimate | Percent Difference |
| Point estimate | 42.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 37.6 |
| upper limit | 46.6 |

Notes:

[14] - 1-sided

| | |
|---|---------------------------------|
| Statistical analysis title | Serotype35B |
| Statistical analysis description: V116-PCV20 Percentage Difference | |
| Comparison groups | Cohort 1 V116 v Cohort 1 PCV20 |
| Number of subjects included in analysis | 2356 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.001 ^[15] |
| Method | Stratified Miettinen & Nurminen |
| Parameter estimate | Percent Difference |
| Point estimate | 53.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 49.6 |
| upper limit | 56.6 |

Notes:

[15] - 1-sided

| | |
|---|---------------------------------|
| Statistical analysis title | Serotype 17F |
| Statistical analysis description: V116-PCV20 Percentage Difference | |
| Comparison groups | Cohort 1 V116 v Cohort 1 PCV20 |
| Number of subjects included in analysis | 2356 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.001 ^[16] |
| Method | Stratified Miettinen & Nurminen |
| Parameter estimate | Percent Difference |
| Point estimate | 66.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 62.8 |
| upper limit | 69.6 |

Notes:

[16] - 1-sided

| | |
|---|---------------------------------|
| Statistical analysis title | Serotype 20A |
| Statistical analysis description: V116-PCV20 Percentage Difference | |
| Comparison groups | Cohort 1 V116 v Cohort 1 PCV20 |
| Number of subjects included in analysis | 2356 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.001 ^[17] |
| Method | Stratified Miettinen & Nurminen |
| Parameter estimate | Percent Difference |
| Point estimate | 57.7 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 54.2 |
| upper limit | 61.1 |

Notes:

[17] - 1-sided

Primary: Serotype specific OPA GMTs in participants 18-49 years and participants 50-64 years for the pneumococcal serotypes contained in V116

| | |
|---|--|
| End point title | Serotype specific OPA GMTs in participants 18-49 years and participants 50-64 years for the pneumococcal serotypes contained in V116 |
| End point description: The serotype specific OPA GMTs for the pneumococcal serotypes in participants 18-49 years and participants 50-64 years treated with V116 only were determined using the MOPA. GMT values were estimated from a cLDA model. The 10 common pneumococcal serotypes in both V116 and PCV20 were as follows: 3, 6A, 7F, 8, 10A, 11A, 12F, 19A, 22F, and 33F. The 11 unique pneumococcal serotypes in V116 were as follows: 9N, 15A, 15C, 16F, 17F, 20A, 23A, 23B, 24F, 31, and 35B. 99999 means per protocol, within group CIs, or any other measures of dispersion, were not determined. The population analyzed was all randomized participants from cohort 1 only, without deviations from the protocol that may substantially affect immunogenicity. Deviations include, but are not limited to the following: missing serology results; and blood draw out of window. | |
| End point type | Primary |
| End point timeframe: Day 30 post-vaccination | |

| End point values | V116 18 to 49 years old | V116 50 to 64 years old | | |
|--|-------------------------|-------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 200 | 589 | | |
| Units: Titer | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Serotype 3 | 308.6 (0 to 99999) | 282.7 (0 to 99999) | | |
| Serotype 6A | 5289.6 (0 to 99999) | 2572.9 (0 to 99999) | | |

| | | | | |
|--------------|----------------------|----------------------|--|--|
| Serotype 7F | 6447.2 (0 to 99999) | 4278.8 (0 to 99999) | | |
| Serotype 8 | 4516.0 (0 to 99999) | 3004.7 (0 to 99999) | | |
| Serotype 9N | 17283.2 (0 to 99999) | 8791.4 (0 to 99999) | | |
| Serotype 10A | 6808.1 (0 to 99999) | 4382.6 (0 to 99999) | | |
| Serotype 11A | 5871.6 (0 to 99999) | 3785.8 (0 to 99999) | | |
| Serotype 12F | 6150.4 (0 to 99999) | 3561.2 (0 to 99999) | | |
| Serotype 15A | 11319.2 (0 to 99999) | 5901.2 (0 to 99999) | | |
| Serotype 15C | 10194.0 (0 to 99999) | 5708.0 (0 to 99999) | | |
| Serotype 16F | 8877.0 (0 to 99999) | 5720.0 (0 to 99999) | | |
| Serotype 17F | 16070.6 (0 to 99999) | 10068.0 (0 to 99999) | | |
| Serotype 19A | 2773.2 (0 to 99999) | 2374.6 (0 to 99999) | | |
| Serotype 20A | 13150.0 (0 to 99999) | 7562.7 (0 to 99999) | | |
| Serotype 22F | 9299.6 (0 to 99999) | 4683.6 (0 to 99999) | | |
| Serotype 23A | 8848.7 (0 to 99999) | 4739.5 (0 to 99999) | | |
| Serotype 23B | 2140.1 (0 to 99999) | 1420.9 (0 to 99999) | | |
| Serotype 24F | 4137.6 (0 to 99999) | 3047.2 (0 to 99999) | | |
| Serotype 31 | 8005.6 (0 to 99999) | 3820.7 (0 to 99999) | | |
| Serotype 33F | 34805.5 (0 to 99999) | 17607.4 (0 to 99999) | | |
| Serotype 35B | 13933.4 (0 to 99999) | 9053.9 (0 to 99999) | | |

Statistical analyses

| Statistical analysis title | Serotype 3 |
|--|---|
| Statistical analysis description: V116 18-49 years/V116 50-64 years GMT Ratio | |
| Comparison groups | V116 18 to 49 years old v V116 50 to 64 years old |
| Number of subjects included in analysis | 789 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.001 ^[18] |
| Method | LDA model |
| Parameter estimate | GMT Ratio |
| Point estimate | 1.09 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.9 |
| upper limit | 1.33 |

Notes:

[18] - 1-sided

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

Statistical analysis description:

V116 18-49 years/V116 50-64 years GMT Ratio

| | |
|---|---|
| Comparison groups | V116 18 to 49 years old v V116 50 to 64 years old |
| Number of subjects included in analysis | 789 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.001 ^[19] |
| Method | LDA model |
| Parameter estimate | GMT Ratio |
| Point estimate | 2.06 |

Confidence interval

| | |
|-------------|---------|
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.61 |
| upper limit | 2.62 |

Notes:

[19] - 1-sided

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

Statistical analysis description:

V116 18-49 years/V116 50-64 years GMT Ratio

| | |
|---|---|
| Comparison groups | V116 18 to 49 years old v V116 50 to 64 years old |
| Number of subjects included in analysis | 789 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.001 ^[20] |
| Method | LDA model |
| Parameter estimate | GMT Ratio |
| Point estimate | 1.51 |

Confidence interval

| | |
|-------------|------------|
| level | Other: 5 % |
| sides | 2-sided |
| lower limit | 1.23 |
| upper limit | 1.84 |

Notes:

[20] - 1-sided

| | |
|-----------------------------------|------------|
| Statistical analysis title | Serotype 8 |
|-----------------------------------|------------|

Statistical analysis description:

V116 18-49 years/V116 50-64 years GMT Ratio

| | |
|-------------------|---|
| Comparison groups | V116 18 to 49 years old v V116 50 to 64 years old |
|-------------------|---|

| | |
|---|-------------------------|
| Number of subjects included in analysis | 789 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.001 ^[21] |
| Method | LDA model |
| Parameter estimate | GMT Ratio |
| Point estimate | 1.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.26 |
| upper limit | 1.79 |

Notes:

[21] - 1-sided

| | |
|-----------------------------------|--------------|
| Statistical analysis title | Serotype 15A |
|-----------------------------------|--------------|

Statistical analysis description:

V116 18-49 years/V116 50-64 years GMT Ratio

| | |
|---|---|
| Comparison groups | V116 18 to 49 years old v V116 50 to 64 years old |
| Number of subjects included in analysis | 789 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.001 ^[22] |
| Method | LDA model |
| Parameter estimate | GMT Ratio |
| Point estimate | 1.92 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.55 |
| upper limit | 2.37 |

Notes:

[22] - 1-sided

| | |
|-----------------------------------|--------------|
| Statistical analysis title | Serotype 10A |
|-----------------------------------|--------------|

Statistical analysis description:

V116 18-49 years/V116 50-64 years GMT Ratio

| | |
|---|---|
| Comparison groups | V116 18 to 49 years old v V116 50 to 64 years old |
| Number of subjects included in analysis | 789 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.001 ^[23] |
| Method | LDA model |
| Parameter estimate | GMT Ratio |
| Point estimate | 1.55 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.26 |
| upper limit | 1.92 |

Notes:

[23] - 1-sided

| | |
|--|---|
| Statistical analysis title | Serotype 11A |
| Statistical analysis description: V116 18-49 years/V116 50-64 years GMT Ratio | |
| Comparison groups | V116 18 to 49 years old v V116 50 to 64 years old |
| Number of subjects included in analysis | 789 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.001 ^[24] |
| Method | LDA model |
| Parameter estimate | GMT Ratio |
| Point estimate | 1.55 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.26 |
| upper limit | 1.91 |

Notes:

[24] - 1-sided

| | |
|--|---|
| Statistical analysis title | Serotype 12F |
| Statistical analysis description: V116 18-49 years/V116 50-64 years GMT Ratio | |
| Comparison groups | V116 18 to 49 years old v V116 50 to 64 years old |
| Number of subjects included in analysis | 789 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.001 ^[25] |
| Method | LDA model |
| Parameter estimate | GMT Ratio |
| Point estimate | 1.73 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.37 |
| upper limit | 2.17 |

Notes:

[25] - 1-sided

| | |
|--|---|
| Statistical analysis title | Serotype 9N |
| Statistical analysis description: V116 18-49 years/V116 50-64 years GMT Ratio | |
| Comparison groups | V116 18 to 49 years old v V116 50 to 64 years old |

| | |
|---|-------------------------|
| Number of subjects included in analysis | 789 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.001 ^[26] |
| Method | LDA model |
| Parameter estimate | GMT Ratio |
| Point estimate | 1.97 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.59 |
| upper limit | 2.43 |

Notes:

[26] - 1-sided

| | |
|-----------------------------------|--------------|
| Statistical analysis title | Serotype 15C |
|-----------------------------------|--------------|

Statistical analysis description:

V116 18-49 years/V116 50-64 years GMT Ratio

| | |
|---|---|
| Comparison groups | V116 18 to 49 years old v V116 50 to 64 years old |
| Number of subjects included in analysis | 789 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.001 ^[27] |
| Method | LDA model |
| Parameter estimate | GMT Ratio |
| Point estimate | 1.79 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.36 |
| upper limit | 2.35 |

Notes:

[27] - 1-sided

| | |
|-----------------------------------|--------------|
| Statistical analysis title | Serotype 16F |
|-----------------------------------|--------------|

Statistical analysis description:

V116 18-49 years/V116 50-64 years GMT Ratio

| | |
|---|---|
| Comparison groups | V116 18 to 49 years old v V116 50 to 64 years old |
| Number of subjects included in analysis | 789 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.001 ^[28] |
| Method | LDA model |
| Parameter estimate | GMT Ratio |
| Point estimate | 1.55 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.26 |
| upper limit | 1.91 |

Notes:

[28] - 1-sided

| | |
|--|---|
| Statistical analysis title | Serotype 17F |
| Statistical analysis description: V116 18-49 years/V116 50-64 years GMT Ratio | |
| Comparison groups | V116 18 to 49 years old v V116 50 to 64 years old |
| Number of subjects included in analysis | 789 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.001 ^[29] |
| Method | LDA model |
| Parameter estimate | GMT Ratio |
| Point estimate | 1.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.26 |
| upper limit | 2.02 |

Notes:

[29] - 1-sided

| | |
|--|---|
| Statistical analysis title | Serotype 19A |
| Statistical analysis description: V116 18-49 years/V116 50-64 years GMT Ratio | |
| Comparison groups | V116 18 to 49 years old v V116 50 to 64 years old |
| Number of subjects included in analysis | 789 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.001 ^[30] |
| Method | LDA model |
| Parameter estimate | GMT Ratio |
| Point estimate | 1.17 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.97 |
| upper limit | 1.4 |

Notes:

[30] - 1-sided

| | |
|--|---|
| Statistical analysis title | Serotype 20A |
| Statistical analysis description: V116 18-49 years/V116 50-64 years GMT Ratio | |
| Comparison groups | V116 18 to 49 years old v V116 50 to 64 years old |

| | |
|---|-------------------------|
| Number of subjects included in analysis | 789 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.001 ^[31] |
| Method | LDA model |
| Parameter estimate | GMT Ratio |
| Point estimate | 1.74 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.39 |
| upper limit | 2.18 |

Notes:

[31] - 1-sided

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

Statistical analysis description:

V116 18-49 years/V116 50-64 years GMT Ratio

| | |
|---|---|
| Comparison groups | V116 18 to 49 years old v V116 50 to 64 years old |
| Number of subjects included in analysis | 789 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.001 ^[32] |
| Method | LDA model |
| Parameter estimate | GMT Ratio |
| Point estimate | 1.99 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.58 |
| upper limit | 2.49 |

Notes:

[32] - 1-sided

| | |
|-----------------------------------|--------------|
| Statistical analysis title | Serotype 23A |
|-----------------------------------|--------------|

Statistical analysis description:

V116 18-49 years/V116 50-64 years GMT Ratio

| | |
|---|---|
| Comparison groups | V116 18 to 49 years old v V116 50 to 64 years old |
| Number of subjects included in analysis | 789 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.001 ^[33] |
| Method | LDA model |
| Parameter estimate | GMT Ratio |
| Point estimate | 1.87 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.43 |
| upper limit | 2.44 |

Notes:

[33] - 1-sided

| | |
|--|---|
| Statistical analysis title | Serotype 23B |
| Statistical analysis description: V116 18-49 years/V116 50-64 years GMT Ratio | |
| Comparison groups | V116 18 to 49 years old v V116 50 to 64 years old |
| Number of subjects included in analysis | 789 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.001 ^[34] |
| Method | LDA model |
| Parameter estimate | GMT Ratio |
| Point estimate | 1.51 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.11 |
| upper limit | 2.04 |

Notes:

[34] - 1-sided

| | |
|--|---|
| Statistical analysis title | Serotype 24F |
| Statistical analysis description: V116 18-49 years/V116 50-64 years GMT Ratio | |
| Comparison groups | V116 18 to 49 years old v V116 50 to 64 years old |
| Number of subjects included in analysis | 789 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.001 ^[35] |
| Method | LDA model |
| Parameter estimate | GMT Ratio |
| Point estimate | 1.36 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.1 |
| upper limit | 1.67 |

Notes:

[35] - 1-sided

| | |
|--|---|
| Statistical analysis title | Serotype 31 |
| Statistical analysis description: V116 18-49 years/V116 50-64 years GMT Ratio | |
| Comparison groups | V116 18 to 49 years old v V116 50 to 64 years old |

| | |
|---|-------------------------|
| Number of subjects included in analysis | 789 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.001 ^[36] |
| Method | LDA model |
| Parameter estimate | GMT Ratio |
| Point estimate | 2.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.63 |
| upper limit | 2.69 |

Notes:

[36] - 1-sided

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

Statistical analysis description:

V116 18-49 years/V116 50-64 years GMT Ratio

| | |
|---|---|
| Comparison groups | V116 18 to 49 years old v V116 50 to 64 years old |
| Number of subjects included in analysis | 789 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.001 ^[37] |
| Method | LDA model |
| Parameter estimate | GMT Ratio |
| Point estimate | 1.98 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.52 |
| upper limit | 2.57 |

Notes:

[37] - 1-sided

| | |
|-----------------------------------|--------------|
| Statistical analysis title | Serotype 35B |
|-----------------------------------|--------------|

Statistical analysis description:

V116 18-49 years/V116 50-64 years GMT Ratio

| | |
|---|---|
| Comparison groups | V116 18 to 49 years old v V116 50 to 64 years old |
| Number of subjects included in analysis | 789 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.001 ^[38] |
| Method | LDA model |
| Parameter estimate | GMT Ratio |
| Point estimate | 1.54 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.26 |
| upper limit | 1.87 |

Notes:

[38] - 1-sided

Secondary: Percentage of participants from Cohort 1 V116 with ≥ 4 -fold change in OPA responses for cross reactive pneumococcal serotypes

| | |
|-----------------|---|
| End point title | Percentage of participants from Cohort 1 V116 with ≥ 4 -fold change in OPA responses for cross reactive pneumococcal serotypes |
|-----------------|---|

End point description:

The percentage of participants with ≥ 4 -fold rise from baseline was determined for Cohort 1 V116 serotypes 6C and 15B, two serotypes which cross react with PCV20. Point estimate and 95% CI are based on the Clopper-Pearson method. A conclusion of acceptability is based on the lower bound of the 95% CI of the percentages of participants with a ≥ 4 -fold rise from baseline being > 50 percentage points (one-sided p-value < 0.025). The population analyzed was all randomized participants from cohort 1 only, without deviations from the protocol that may substantially affect immunogenicity. Deviations include, but are not limited to the following: missing serology results; and blood draw out of window. Per protocol, participants treated with PCV20, and V116 Cohort 2 were not analyzed in this outcome measure. For arm PCV20: Cohort 1 99999 means per protocol, within group CIs, or any other measures of dispersion, were not determined.

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

End point timeframe:

Baseline and Day 30 post-vaccination

| End point values | Cohort 1 V116 | Cohort 1 PCV20 | Cohort 2 V116 | Cohort 2 PCV20 |
|-----------------------------------|---------------------|----------------------|-------------------|-------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 1179 | 1177 ^[39] | 0 ^[40] | 0 ^[41] |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| Serotype 6C | 49.3 (46.0 to 52.6) | 0 (0 to 99999) | (to) | (to) |
| Serotype 15B | 64.7 (61.4 to 67.8) | 0 (0 to 99999) | (to) | (to) |

Notes:

[39] - Per protocol, Cohort 1: PCV20 were not analyzed in this endpoint.

[40] - Per protocol, Cohort 2 were not analyzed in this endpoint.

[41] - Per protocol, Cohort 2 were not analyzed in this endpoint.

Statistical analyses

| | |
|----------------------------|--------------|
| Statistical analysis title | Serotype 15B |
|----------------------------|--------------|

Statistical analysis description:

Serotype 15B

| | |
|---|--------------------------------|
| Comparison groups | Cohort 1 V116 v Cohort 1 PCV20 |
| Number of subjects included in analysis | 2356 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.001 ^[42] |
| Method | Clopper-Pearson method. |

Notes:

[42] - 1-sided

| | |
|--|--------------------------------|
| Statistical analysis title | Serotype 6C |
| Statistical analysis description: Serotype 6C | |
| Comparison groups | Cohort 1 V116 v Cohort 1 PCV20 |
| Number of subjects included in analysis | 2356 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.667 ^[43] |
| Method | Clopper-Pearson method. |
| Notes: [43] - 1-sided | |

Secondary: Serotype specific OPA GMTs for cross reactive pneumococcal serotypes in adults 50 to 64 years of age from Cohort 1 and adults 18 to 49 years of age from Cohort 2

| | |
|--|---|
| End point title | Serotype specific OPA GMTs for cross reactive pneumococcal serotypes in adults 50 to 64 years of age from Cohort 1 and adults 18 to 49 years of age from Cohort 2 |
| End point description: The serotype specific OPA GMTs for the pneumococcal serotypes in participants 18-49 years and participants 50-64 years treated with V116 only were determined using the MOPA for serotypes 6C and 15B which cross react with PCV20. GMT values were estimated from a LDA model. 99999 means per protocol, within group CIs, or any other measures of dispersion, were not determined. The population analyzed was all randomized participants from cohort 1 only, without deviations from the protocol that may substantially affect immunogenicity. Deviations include, but are not limited to the following: missing serology results; and blood draw out of window. | |
| End point type | Secondary |
| End point timeframe: Day 30 post-vaccination | |

| End point values | V116 18 to 49 years old | V116 50 to 64 years old | | |
|--|-------------------------|-------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 200 | 589 | | |
| Units: Titer | | | | |
| geometric mean (confidence interval 95%) | | | | |
| 6C | 2577.2 (0 to 99999) | 1254.7 (0 to 99999) | | |
| 15B | 10976.7 (0 to 99999) | 5438.9 (0 to 99999) | | |

Statistical analyses

| | |
|--|---|
| Statistical analysis title | Serotype 15B |
| Statistical analysis description: V116 18-49 years/V116 50-64 years GMT ratio | |
| Comparison groups | V116 18 to 49 years old v V116 50 to 64 years old |

| | |
|---|-------------------------|
| Number of subjects included in analysis | 789 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.001 ^[44] |
| Method | LDA model |
| Parameter estimate | GMT |
| Point estimate | 2.02 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.57 |
| upper limit | 2.6 |

Notes:

[44] - 1-sided

| | |
|--|---|
| Statistical analysis title | Serotype 6C |
| Statistical analysis description: V116 18-49 years/V116 50-64 years GMT Ratio | |
| Comparison groups | V116 18 to 49 years old v V116 50 to 64 years old |
| Number of subjects included in analysis | 789 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | GMT Ratio |
| Point estimate | 2.05 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.52 |
| upper limit | 2.77 |

Secondary: Serotype specific Immunoglobulin (IgG) geometric mean concentrations (GMCs) in Cohort 1 only, for the pneumococcal serotypes contained in V116 and PCV20

| | |
|-----------------|--|
| End point title | Serotype specific Immunoglobulin (IgG) geometric mean concentrations (GMCs) in Cohort 1 only, for the pneumococcal serotypes contained in V116 and PCV20 |
|-----------------|--|

End point description:

The serotype specific IgG GMCs for the pneumococcal serotypes in cohort 1 of V116 and PCV20 only were determined using pneumococcal electrochemiluminescence (PnECL). GMC values were estimated from a cLDA model. Per protocol, within group CIs or any other measures of dispersion were not planned or determined. The 10 common pneumococcal serotypes in both V116 and PCV20 were as follows: 3, 6A, 7F, 8, 10A, 11A, 12F, 19A, 22F, and 33F. The 11 unique pneumococcal serotypes in V116 were as follows: 9N, 15A, 15C, 16F, 17F, 20A, 23A, 23B, 24F, 31, and 35B. 99999 means per protocol, within group CIs, or any other measures of dispersion, were not determined. The population analyzed was all randomized participants from cohort 1 only, without deviations from the protocol that may substantially affect immunogenicity. Deviations include, but are not limited to the following: missing serology results; and blood draw out of window.

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

End point timeframe:

Day 30 post-vaccination

| End point values | Cohort 1 V116 | Cohort 1 PCV20 | Cohort 2 V116 | Cohort 2 PCV20 |
|--|--------------------|--------------------|-------------------|-------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 1179 | 1177 | 0 ^[45] | 0 ^[46] |
| Units: µg/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Serotype 3 | 0.78 (0 to 99999) | 0.53 (0 to 99999) | (to) | (to) |
| Serotype 6A | 4.30 (0 to 99999) | 5.45 (0 to 99999) | (to) | (to) |
| Serotype 7F | 6.97 (0 to 99999) | 6.57 (0 to 99999) | (to) | (to) |
| Serotype 8 | 10.02 (0 to 99999) | 7.00 (0 to 99999) | (to) | (to) |
| Serotype 10A | 11.98 (0 to 99999) | 14.66 (0 to 99999) | (to) | (to) |
| Serotype 11A | 7.20 (0 to 99999) | 5.87 (0 to 99999) | (to) | (to) |
| Serotype 12F | 1.73 (0 to 99999) | 1.57 (0 to 99999) | (to) | (to) |
| Serotype 19A | 8.39 (0 to 99999) | 12.02 (0 to 99999) | (to) | (to) |
| Serotype 22F | 4.39 (0 to 99999) | 5.48 (0 to 99999) | (to) | (to) |
| Serotype 33F | 13.81 (0 to 99999) | 13.02 (0 to 99999) | (to) | (to) |
| Serotype 9N | 7.72 (0 to 99999) | 1.43 (0 to 99999) | (to) | (to) |
| Serotype15A | 13.88 (0 to 99999) | 2.04 (0 to 99999) | (to) | (to) |
| Serotype 15C | 12.39 (0 to 99999) | 5.04 (0 to 99999) | (to) | (to) |
| Serotype 16F | 2.86 (0 to 99999) | 0.33 (0 to 99999) | (to) | (to) |
| Serotype 17F | 14.16 (0 to 99999) | 0.84 (0 to 99999) | (to) | (to) |
| Serotype 20A | 19.03 (0 to 99999) | 1.47 (0 to 99999) | (to) | (to) |
| Serotype 23A | 3.78 (0 to 99999) | 0.59 (0 to 99999) | (to) | (to) |
| Serotype 23B | 5.13 (0 to 99999) | 1.58 (0 to 99999) | (to) | (to) |
| Serotype 24F | 6.87 (0 to 99999) | 0.33 (0 to 99999) | (to) | (to) |
| Serotype 31 | 3.07 (0 to 99999) | 0.27 (0 to 99999) | (to) | (to) |
| Serotype 35B | 19.98 (0 to 99999) | 1.41 (0 to 99999) | (to) | (to) |

Notes:

[45] - Per protocol, Cohort 2 were not analyzed in this endpoint.

[46] - Per protocol, Cohort 2 were not analyzed in this endpoint.

Statistical analyses

| | |
|---|--------------------------------|
| Statistical analysis title | Serotype 7F |
| Statistical analysis description: V116/PCV20 GMC Ratio | |
| Comparison groups | Cohort 1 V116 v Cohort 1 PCV20 |
| Number of subjects included in analysis | 2356 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | GMC Ratio |
| Point estimate | 1.06 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.95 |
| upper limit | 1.18 |

| | |
|---|--------------------------------|
| Statistical analysis title | Serotype 6A |
| Statistical analysis description: V116/PCV20 GMC Ratio | |
| Comparison groups | Cohort 1 V116 v Cohort 1 PCV20 |
| Number of subjects included in analysis | 2356 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | GMC Ratio |
| Point estimate | 0.79 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.7 |
| upper limit | 0.89 |

| | |
|---|--------------------------------|
| Statistical analysis title | Serotype 3 |
| Statistical analysis description: V116/PCV20 GMC Ratio | |
| Comparison groups | Cohort 1 V116 v Cohort 1 PCV20 |
| Number of subjects included in analysis | 2356 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | GMC Ratio |
| Point estimate | 1.47 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.35 |
| upper limit | 1.6 |

| | |
|---|--------------------------------|
| Statistical analysis title | Serotype 8 |
| Statistical analysis description: V116/PCV20 GMC Ratio | |
| Comparison groups | Cohort 1 V116 v Cohort 1 PCV20 |
| Number of subjects included in analysis | 2356 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | GMC Ratio |
| Point estimate | 1.43 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.29 |
| upper limit | 1.59 |

| | |
|---|--------------------------------|
| Statistical analysis title | Serotype 10A |
| Statistical analysis description: V116/PCV20 GMC Ratio | |
| Comparison groups | Cohort 1 V116 v Cohort 1 PCV20 |
| Number of subjects included in analysis | 2356 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | GMC Ratio |
| Point estimate | 0.82 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.72 |
| upper limit | 0.92 |

| | |
|---|--------------------------------|
| Statistical analysis title | Serotype 11A |
| Statistical analysis description: V116/PCV20 GMC Ratio | |
| Comparison groups | Cohort 1 V116 v Cohort 1 PCV20 |
| Number of subjects included in analysis | 2356 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | GMC Ratio |
| Point estimate | 1.23 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.11 |
| upper limit | 1.36 |

| | |
|---|--------------------------------|
| Statistical analysis title | Serotype 12F |
| Statistical analysis description: V116/PCV20 GMC Ratio | |
| Comparison groups | Cohort 1 V116 v Cohort 1 PCV20 |
| Number of subjects included in analysis | 2356 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | GMC Ratio |
| Point estimate | 1.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.96 |
| upper limit | 1.26 |

| | |
|---|--------------------------------|
| Statistical analysis title | Serotype 33F |
| Statistical analysis description: V116/PCV20 GMC Ratio | |
| Comparison groups | Cohort 1 V116 v Cohort 1 PCV20 |
| Number of subjects included in analysis | 2356 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | GMC Ratio |
| Point estimate | 1.06 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.95 |
| upper limit | 1.18 |

| | |
|---|--------------------------------|
| Statistical analysis title | Serotype 22F |
| Statistical analysis description: V116/PCV20 GMC Ratio | |
| Comparison groups | Cohort 1 V116 v Cohort 1 PCV20 |

| | |
|---|---------------|
| Number of subjects included in analysis | 2356 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | GMC Ratio |
| Point estimate | 0.8 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.72 |
| upper limit | 0.9 |

| | |
|---|--------------------------------|
| Statistical analysis title | Serotype 19A |
| Statistical analysis description: V116/PCV20 GMC Ratio | |
| Comparison groups | Cohort 1 V116 v Cohort 1 PCV20 |
| Number of subjects included in analysis | 2356 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | GMC Ratio |
| Point estimate | 0.7 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.63 |
| upper limit | 0.77 |

| | |
|---|--------------------------------|
| Statistical analysis title | Serotype 9N |
| Statistical analysis description: V116/PCV20 GMC Ratio | |
| Comparison groups | Cohort 1 V116 v Cohort 1 PCV20 |
| Number of subjects included in analysis | 2356 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | GMC Ratio |
| Point estimate | 5.41 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 4.82 |
| upper limit | 6.06 |

| | |
|---|--------------|
| Statistical analysis title | Serotype 15A |
| Statistical analysis description: V116/PCV20 GMC Ratio | |

| | |
|---|--------------------------------|
| Comparison groups | Cohort 1 V116 v Cohort 1 PCV20 |
| Number of subjects included in analysis | 2356 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | GMC Ratio |
| Point estimate | 6.79 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 6.03 |
| upper limit | 7.64 |

| | |
|---|--------------------------------|
| Statistical analysis title | Serotype 15C |
| Statistical analysis description: V116/PCV20 GMC Ratio | |
| Comparison groups | Cohort 1 V116 v Cohort 1 PCV20 |
| Number of subjects included in analysis | 2356 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | GMC Ratio |
| Point estimate | 2.46 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 2.17 |
| upper limit | 2.79 |

| | |
|---|--------------------------------|
| Statistical analysis title | Serotype 16F |
| Statistical analysis description: V116/PCV20 GMC Ratio | |
| Comparison groups | Cohort 1 V116 v Cohort 1 PCV20 |
| Number of subjects included in analysis | 2356 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | GMC Ratio |
| Point estimate | 8.75 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 7.95 |
| upper limit | 9.64 |

| | |
|-----------------------------------|--------------|
| Statistical analysis title | Serotype 17F |
|-----------------------------------|--------------|

| | |
|---|--------------------------------|
| Statistical analysis description: | |
| V116/PCV20 GMC Ratio | |
| Comparison groups | Cohort 1 V116 v Cohort 1 PCV20 |
| Number of subjects included in analysis | 2356 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | GMC Ratio |
| Point estimate | 16.75 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 15.25 |
| upper limit | 18.41 |

| | |
|---|--------------------------------|
| Statistical analysis title | Serotype 20A |
| Statistical analysis description: | |
| V116/PCV20 GMC Ratio | |
| Comparison groups | Cohort 1 V116 v Cohort 1 PCV20 |
| Number of subjects included in analysis | 2356 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | GMC Ratio |
| Point estimate | 12.92 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 11.81 |
| upper limit | 14.13 |

| | |
|---|--------------------------------|
| Statistical analysis title | Serotype 23A |
| Statistical analysis description: | |
| V116/PCV20 GMC Ratio | |
| Comparison groups | Cohort 1 V116 v Cohort 1 PCV20 |
| Number of subjects included in analysis | 2356 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | GMC Ratio |
| Point estimate | 6.42 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 5.69 |
| upper limit | 7.24 |

| | |
|---|--------------------------------|
| Statistical analysis title | Serotype 23B |
| Statistical analysis description: V116/PCV20 GMC Ratio | |
| Comparison groups | Cohort 1 V116 v Cohort 1 PCV20 |
| Number of subjects included in analysis | 2356 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | GMC Ratio |
| Point estimate | 3.25 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 2.91 |
| upper limit | 3.64 |

| | |
|---|--------------------------------|
| Statistical analysis title | Serotype 24F |
| Statistical analysis description: V116/PCV20 GMC Ratio | |
| Comparison groups | Cohort 1 V116 v Cohort 1 PCV20 |
| Number of subjects included in analysis | 2356 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | GMC Ratio |
| Point estimate | 21.08 |
| Confidence interval | |
| level | Other: 85 % |
| sides | 2-sided |
| lower limit | 18.97 |
| upper limit | 23.43 |

| | |
|---|--------------------------------|
| Statistical analysis title | Serotype 31 |
| Statistical analysis description: V116/PCV20 GMC Ratio | |
| Comparison groups | Cohort 1 V116 v Cohort 1 PCV20 |
| Number of subjects included in analysis | 2356 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | GMC Ratio |
| Point estimate | 11.31 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 10.36 |
| upper limit | 12.34 |

| | |
|---|--------------------------------|
| Statistical analysis title | Serotype 35B |
| Statistical analysis description: V116/PCV20 GMC Ratio | |
| Comparison groups | Cohort 1 V116 v Cohort 1 PCV20 |
| Number of subjects included in analysis | 2356 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | GMC Ratio |
| Point estimate | 14.13 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 12.97 |
| upper limit | 15.4 |

Secondary: Geometric mean fold change from baseline in OPA GMTs in Cohort 1 for the pneumococcal serotypes contained in V116 and PCV20

| | |
|-----------------|---|
| End point title | Geometric mean fold change from baseline in OPA GMTs in Cohort 1 for the pneumococcal serotypes contained in V116 and PCV20 |
|-----------------|---|

End point description:

The geometric mean fold rise (GMFR) from baseline in serotype specific OPA GMTs for cohort 1 was determined using MOPA. The within-group 95% CIs were obtained by exponentiating the CIs of the mean of the natural log values based on the t-distribution. The 10 common pneumococcal serotypes in both V116 and PCV20 were as follows: 3, 6A, 7F, 8, 10A, 11A, 12F, 19A, 22F, and 33F. The 11 unique pneumococcal serotypes in V116 were as follows: 9N, 15A, 15C, 16F, 17F, 20A, 23A, 23B, 24F, 31, and 35B. Per protocol, Cohort 2 were not analyzed in this outcome measure.

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

End point timeframe:

Baseline and Day 30 post-vaccination

| End point values | Cohort 1 V116 | Cohort 1 PCV20 | Cohort 2 V116 | Cohort 2 PCV20 |
|--|---------------------|---------------------|-------------------|-------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 1179 | 1177 | 0 ^[47] | 0 ^[48] |
| Units: GMFR | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Serotype 3 | 8.4 (7.7 to 9.1) | 5.4 (5.0 to 5.8) | (to) | (to) |
| Serotype 6A | 18.1 (16.2 to 20.2) | 22.6 (20.1 to 25.5) | (to) | (to) |
| Serotype 7F | 16.5 (14.4 to 18.8) | 14.7 (12.9 to 16.8) | (to) | (to) |
| Serotype 8 | 22.0 (19.3 to 25.0) | 14.2 (12.5 to 16.2) | (to) | (to) |
| Serotype 10A | 16.7 (14.8 to 18.9) | 20.8 (18.3 to 23.8) | (to) | (to) |

| | | | | |
|--------------|---------------------|---------------------|--------|--------|
| Serotype 11A | 17.4 (15.1 to 20.0) | 11.6 (10.1 to 13.3) | (to) | (to) |
| Serotype 12F | 77.4 (68.5 to 87.4) | 73.5 (64.8 to 83.4) | (to) | (to) |
| Serotype 19A | 8.6 (7.7 to 9.5) | 11.0 (9.9 to 12.2) | (to) | (to) |
| Serotype 22F | 19.1 (16.6 to 22.1) | 25.5 (21.9 to 29.8) | (to) | (to) |
| Serotype 33F | 9.9 (8.9 to 11.1) | 8.5 (7.6 to 9.5) | (to) | (to) |
| Serotype 9N | 8.9 (8.0 to 9.9) | 2.0 (1.9 to 2.2) | (to) | (to) |
| Serotype 15A | 9.4 (8.2 to 10.8) | 3.1 (2.7 to 3.5) | (to) | (to) |
| Serotype 15C | 38.0 (33.3 to 43.3) | 20.3 (17.8 to 23.1) | (to) | (to) |
| Serotype 16F | 9.5 (8.7 to 10.4) | 1.9 (1.7 to 2.0) | (to) | (to) |
| Serotype 17F | 17.3 (15.3 to 19.7) | 1.2 (1.1 to 1.3) | (to) | (to) |
| Serotype 20A | 10.3 (9.2 to 11.4) | 1.2 (1.1 to 1.2) | (to) | (to) |
| Serotype 23A | 21.8 (19.0 to 25.0) | 3.1 (2.7 to 3.6) | (to) | (to) |
| Serotype 23B | 51.4 (45.3 to 58.2) | 6.1 (5.4 to 6.9) | (to) | (to) |
| Serotype 24F | 29.0 (25.6 to 32.8) | 1.1 (1.0 to 1.1) | (to) | (to) |
| Serotype 31 | 28.7 (24.9 to 33.1) | 1.5 (1.4 to 1.7) | (to) | (to) |
| Serotype 35B | 7.2 (6.5 to 7.9) | 1.2 (1.1 to 1.2) | (to) | (to) |

Notes:

[47] - Per protocol Cohort 2 was not analyzed for this endpoint.

[48] - Per protocol Cohort 2 was not analyzed for this endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric mean fold change from baseline in IgG antibody GMCs in Cohort 1 for the pneumococcal serotypes contained in V116 and PCV20

| | |
|-----------------|--|
| End point title | Geometric mean fold change from baseline in IgG antibody GMCs in Cohort 1 for the pneumococcal serotypes contained in V116 and PCV20 |
|-----------------|--|

End point description:

The GMFR from baseline in serotype specific IgG antibody GMCs for cohort 1 was determined using PnECL. The within-group 95% CIs were obtained by exponentiating the CIs of the mean of the natural log values based on the t-distribution. The 10 common pneumococcal serotypes in both V116 and PCV20 were as follows: 3, 6A, 7F, 8, 10A, 11A, 12F, 19A, 22F, and 33F. The 11 unique pneumococcal serotypes in V116 were as follows: 9N, 15A, 15C, 16F, 17F, 20A, 23A, 23B, 24F, 31, and 35B. Per protocol, Cohort 2 were not analyzed in this outcome measure.

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

End point timeframe:

Baseline and Day 30 post-vaccination

| End point values | Cohort 1 V116 | Cohort 1 PCV20 | Cohort 2 V116 | Cohort 2 PCV20 |
|--|---------------------|---------------------|-------------------|-------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 1179 | 1177 | 0 ^[49] | 0 ^[50] |
| Units: GMFR | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Serotype 3 | 5.1 (4.8 to 5.4) | 3.5 (3.3 to 3.7) | (to) | (to) |
| Serotype 6A | 12.2 (11.1 to 13.5) | 15.1 (13.8 to 16.6) | (to) | (to) |
| Serotype 7F | 12.5 (11.5 to 13.7) | 12.2 (11.2 to 13.4) | (to) | (to) |
| Serotype 8 | 12.6 (11.5 to 13.8) | 8.8 (8.0 to 9.6) | (to) | (to) |
| Serotype 10A | 15.4 (14.1 to 16.9) | 19.2 (17.4 to 21.1) | (to) | (to) |
| Serotype 11A | 8.7 (8.1 to 9.5) | 7.1 (6.5 to 7.7) | (to) | (to) |
| Serotype 12F | 13.1 (11.8 to 14.4) | 12.1 (11.0 to 13.5) | (to) | (to) |
| Serotype 19A | 5.4 (5.0 to 5.8) | 7.7 (7.1 to 8.4) | (to) | (to) |
| Serotype 22F | 12.7 (11.6 to 13.9) | 16.3 (14.8 to 17.9) | (to) | (to) |
| Serotype 33F | 9.6 (8.8 to 10.5) | 9.1 (8.3 to 9.9) | (to) | (to) |
| Serotype 9N | 15.0 (13.6 to 16.5) | 2.7 (2.5 to 2.9) | (to) | (to) |
| Serotype 15A | 22.3 (20.3 to 24.4) | 3.4 (3.1 to 3.7) | (to) | (to) |
| Serotype 15C | 19.8 (17.9 to 21.8) | 8.2 (7.4 to 9.0) | (to) | (to) |
| Serotype 16F | 13.3 (12.3 to 14.4) | 1.6 (1.5 to 1.7) | (to) | (to) |
| Serotype 17F | 19.8 (18.0 to 21.7) | 1.2 (1.1 to 1.3) | (to) | (to) |
| Serotype 20A | 11.7 (10.8 to 12.8) | 0.9 (0.9 to 1.0) | (to) | (to) |
| Serotype 23A | 17.8 (16.3 to 19.5) | 2.9 (2.6 to 3.1) | (to) | (to) |
| Serotype 23B | 12.1 (11.1 to 13.3) | 3.8 (3.5 to 4.1) | (to) | (to) |
| Serotype 24F | 21.2 (19.3 to 23.4) | 1.1 (1.0 to 1.1) | (to) | (to) |
| Serotype 31 | 13.0 (12.0 to 14.0) | 1.2 (1.2 to 1.3) | (to) | (to) |
| Serotype 35B | 14.7 (13.6 to 16.0) | 1.0 (1.0 to 1.1) | (to) | (to) |

Notes:

[49] - Per protocol Cohort 2 was not analyzed for this endpoint.

[50] - Per protocol Cohort 2 was not analyzed for this endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with ≥ 4 -fold change from baseline in IgG antibody GMCs in Cohort 1 for the pneumococcal serotypes contained in V116 and PCV20

| | |
|-----------------|---|
| End point title | Percentage of participants with ≥ 4 -fold change from baseline in IgG antibody GMCs in Cohort 1 for the pneumococcal serotypes |
|-----------------|---|

End point description:

Percentage of participants with ≥ 4 -fold rise from baseline in serotype specific IgG antibody GMCs for cohort 1 was determined using PnECL. The within-group 95% CIs were based on the exact binomial method proposed by Clopper and Pearson. The 10 common pneumococcal serotypes in both V116 and PCV20 were as follows: 3, 6A, 7F, 8, 10A, 11A, 12F, 19A, 22F, and 33F. The 11 unique pneumococcal serotypes in V116 were as follows: 9N, 15A, 15C, 16F, 17F, 20A, 23A, 23B, 24F, 31, and 35B. Per protocol, Cohort 2 were not analyzed in this outcome measure.

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

End point timeframe:

Baseline and Day 30 post-vaccination

| End point values | Cohort 1 V116 | Cohort 1 PCV20 | Cohort 2 V116 | Cohort 2 PCV20 |
|-----------------------------------|---------------------|---------------------|-------------------|-------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 1179 | 1177 | 0 ^[51] | 0 ^[52] |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| Serotype 3 | 56.5 (53.5 to 59.4) | 41.0 (38.0 to 44.0) | (to) | (to) |
| Serotype 6A | 73.1 (70.4 to 75.7) | 79.7 (77.2 to 82.1) | (to) | (to) |
| Serotype 7F | 76.4 (73.8 to 78.9) | 75.8 (73.2 to 78.4) | (to) | (to) |
| Serotype 8 | 75.8 (73.1 to 78.3) | 67.8 (64.9 to 70.6) | (to) | (to) |
| Serotype 10A | 80.3 (77.8 to 82.6) | 82.0 (79.5 to 84.2) | (to) | (to) |
| Serotype 11A | 71.1 (68.4 to 73.8) | 62.7 (59.8 to 65.6) | (to) | (to) |
| Serotype 12F | 74.2 (71.5 to 76.7) | 71.4 (68.6 to 74.1) | (to) | (to) |
| Serotype 19A | 55.6 (52.6 to 58.5) | 65.0 (62.0 to 67.8) | (to) | (to) |
| Serotype 22F | 76.8 (74.2 to 79.3) | 78.5 (76.0 to 81.0) | (to) | (to) |
| Serotype 33F | 71.6 (68.8 to 74.2) | 66.7 (63.8 to 69.6) | (to) | (to) |
| Serotype 9N | 77.9 (75.3 to 80.3) | 29.4 (26.7 to 32.2) | (to) | (to) |
| Serotype 15A | 85.7 (83.5 to 87.8) | 37.7 (34.8 to 40.7) | (to) | (to) |
| Serotype 15C | 81.4 (78.9 to 83.6) | 63.2 (60.2 to 66.1) | (to) | (to) |
| Serotype 16F | 81.4 (78.9 to 83.6) | 11.8 (10.0 to 13.9) | (to) | (to) |
| Serotype 17F | 84.5 (82.2 to 86.6) | 4.3 (3.1 to 5.7) | (to) | (to) |
| Serotype 20A | 74.7 (72.1 to 77.3) | 1.3 (0.7 to 2.2) | (to) | (to) |
| Serotype 23A | 85.5 (83.3 to 87.6) | 29.4 (26.7 to 32.2) | (to) | (to) |
| Serotype 23B | 76.1 (73.4 to 78.6) | 42.2 (39.3 to 45.2) | (to) | (to) |
| Serotype 24F | 84.0 (81.7 to 86.1) | 2.3 (1.5 to 3.4) | (to) | (to) |

| | | | | |
|--------------|---------------------|------------------|--------|--------|
| Serotype 31 | 81.1 (78.6 to 83.4) | 3.9 (2.8 to 5.2) | (to) | (to) |
| Serotype 35B | 83.1 (80.8 to 85.3) | 3.3 (2.3 to 4.5) | (to) | (to) |

Notes:

[51] - Per protocol Cohort 2 was not analyzed for this endpoint.

[52] - Per protocol Cohort 2 was not analyzed for this endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with ≥ 4 -fold change from baseline in OPA GMTs in Cohort 1 for the pneumococcal serotypes contained in V116 and PCV20

| | |
|-----------------|--|
| End point title | Percentage of participants with ≥ 4 -fold change from baseline in OPA GMTs in Cohort 1 for the pneumococcal serotypes contained in V116 and PCV20 |
|-----------------|--|

End point description:

Percentage of participants with ≥ 4 -fold rise from baseline in OPA GMTs in Cohort 1 was determined using MOPA. The within-group 95% CIs were based on the exact binomial method proposed by Clopper and Pearson. The 10 common pneumococcal serotypes in both V116 and PCV20 were as follows: 3, 6A, 7F, 8, 10A, 11A, 12F, 19A, 22F, and 33F. The 11 unique pneumococcal serotypes in V116 were as follows: 9N, 15A, 15C, 16F, 17F, 20A, 23A, 23B, 24F, 31, and 35B. Per protocol, Cohort 2 were not analyzed in this outcome measure.

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

End point timeframe:

Baseline and Day 30 post-vaccination

| End point values | Cohort 1 V116 | Cohort 1 PCV20 | Cohort 2 V116 | Cohort 2 PCV20 |
|-----------------------------------|---------------------|---------------------|-------------------|-------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 1179 | 1177 | 0 ^[53] | 0 ^[54] |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| Serotype 3 | 71.3 (68.4 to 74.2) | 59.1 (55.9 to 62.3) | (to) | (to) |
| Serotype 6A | 76.8 (74.0 to 79.5) | 79.9 (77.2 to 82.4) | (to) | (to) |
| Serotype 7F | 71.0 (68.1 to 73.9) | 65.9 (62.8 to 68.9) | (to) | (to) |
| Serotype 8 | 75.8 (73.0 to 78.4) | 67.4 (64.3 to 70.3) | (to) | (to) |
| Serotype 10A | 71.9 (69.0 to 74.6) | 74.1 (71.3 to 76.9) | (to) | (to) |
| Serotype11A | 70.0 (66.9 to 73.0) | 61.5 (58.2 to 64.7) | (to) | (to) |
| Serotype 12F | 89.0 (87.0 to 90.9) | 87.1 (84.9 to 89.1) | (to) | (to) |
| Serotype 19A | 64.4 (61.3 to 67.3) | 70.2 (67.2 to 73.0) | (to) | (to) |
| Serotype 22F | 70.5 (67.5 to 73.4) | 74.4 (71.5 to 77.2) | (to) | (to) |
| Serotype 33F | 67.7 (64.6 to 70.7) | 61.5 (58.3 to 64.6) | (to) | (to) |
| Serotype 9N | 64.7 (61.5 to 67.8) | 19.9 (17.5 to 22.6) | (to) | (to) |

| | | | | |
|--------------|---------------------|---------------------|--------|--------|
| Serotype 15A | 66.7 (63.0 to 70.2) | 35.8 (32.3 to 39.5) | (to) | (to) |
| Serotype 15C | 83.4 (80.9 to 85.7) | 74.2 (71.2 to 76.9) | (to) | (to) |
| Serotype 16F | 71.9 (68.8 to 74.8) | 20.8 (18.3 to 23.5) | (to) | (to) |
| Serotype 17F | 75.8 (72.7 to 78.6) | 9.5 (7.7 to 11.5) | (to) | (to) |
| Serotype 20A | 67.3 (64.3 to 70.2) | 9.6 (7.8 to 11.6) | (to) | (to) |
| Serotype 23A | 78.9 (75.8 to 81.7) | 36.8 (33.3 to 40.4) | (to) | (to) |
| Serotype 23B | 85.5 (83.2 to 87.6) | 49.6 (46.4 to 52.7) | (to) | (to) |
| Serotype 24F | 80.5 (77.8 to 83.0) | 6.3 (4.8 to 8.1) | (to) | (to) |
| Serotype 31 | 76.5 (73.6 to 79.3) | 17.9 (15.5 to 20.5) | (to) | (to) |
| Serotype 35B | 60.0 (56.7 to 63.2) | 6.8 (5.3 to 8.5) | (to) | (to) |

Notes:

[53] - Per protocol Cohort 2 was not analyzed for this endpoint.

[54] - Per protocol Cohort 2 was not analyzed for this endpoint.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All-cause mortality (ACM): Randomization up to 194 days post-vaccination. Serious adverse events (SAEs): Treatment (Day 1) up to 194 days post-vaccination. Non-serious AEs (NSAEs): Treatment (Day 1) up to 30 days post-vaccination.

Adverse event reporting additional description:

ACM for Cohorts 1 and 2: randomized participants. ACM for Unplanned arm: participants randomized to both V116 and PCV20. The SAE and NSAE for Cohorts 1 and 2 was the APaT. The SAEs and NSAEs for the Unplanned arm: participants excluded from the APaT. ACMs or AEs for the Unplanned arm were reported as zero due to the risk of identification..

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

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 26.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|----------------|
| Reporting group title | Cohort 1: V116 |
|-----------------------|----------------|

Reporting group description:

Pneumococcal vaccine-naïve adult participants (≥50 years of age) receive a single dose of V116 on Day 1.

| | |
|-----------------------|-----------------|
| Reporting group title | Cohort 1: PCV20 |
|-----------------------|-----------------|

Reporting group description:

Pneumococcal vaccine-naïve adult participants (≥50 years of age) receive a single dose of PCV20 on Day 1.

| | |
|-----------------------|------------------------|
| Reporting group title | Unplanned Participants |
|-----------------------|------------------------|

Reporting group description:

Participants with unplanned randomization and unplanned treatment with both V116 and PCV20.

| | |
|-----------------------|-----------------|
| Reporting group title | Cohort 2: PCV20 |
|-----------------------|-----------------|

Reporting group description:

Pneumococcal vaccine-naïve adult participants (18 to 49 years of age) receive a single dose of PCV20 on Day 1.

| | |
|-----------------------|----------------|
| Reporting group title | Cohort 2: V116 |
|-----------------------|----------------|

Reporting group description:

Pneumococcal vaccine-naïve adult participants (18 to 49 years of age) receive a single dose of V116 on Day 1.

| Serious adverse events | Cohort 1: V116 | Cohort 1: PCV20 | Unplanned Participants |
|---|-------------------|-------------------|------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 19 / 1177 (1.61%) | 24 / 1175 (2.04%) | 0 / 2 (0.00%) |
| number of deaths (all causes) | 4 | 2 | 0 |
| number of deaths resulting from adverse events | 4 | 2 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Rectal adenocarcinoma | | | |

| | | | |
|--|------------------|------------------|---------------|
| subjects affected / exposed | 1 / 1177 (0.08%) | 0 / 1175 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Prostate cancer | | | |
| subjects affected / exposed | 0 / 1177 (0.00%) | 1 / 1175 (0.09%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Invasive ductal breast carcinoma | | | |
| subjects affected / exposed | 1 / 1177 (0.08%) | 0 / 1175 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 1177 (0.00%) | 1 / 1175 (0.09%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune system disorders | | | |
| Drug hypersensitivity | | | |
| subjects affected / exposed | 0 / 1177 (0.00%) | 1 / 1175 (0.09%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute respiratory failure | | | |
| subjects affected / exposed | 1 / 1177 (0.08%) | 0 / 1175 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dyspnoea | | | |
| subjects affected / exposed | 1 / 1177 (0.08%) | 0 / 1175 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Alcohol withdrawal syndrome | | | |

| | | | |
|---|------------------|------------------|---------------|
| subjects affected / exposed | 0 / 1177 (0.00%) | 1 / 1175 (0.09%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Alcoholism | | | |
| subjects affected / exposed | 1 / 1177 (0.08%) | 0 / 1175 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Delirium tremens | | | |
| subjects affected / exposed | 1 / 1177 (0.08%) | 0 / 1175 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Product issues | | | |
| Device occlusion | | | |
| subjects affected / exposed | 1 / 1177 (0.08%) | 0 / 1175 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Brain contusion | | | |
| subjects affected / exposed | 0 / 1177 (0.00%) | 1 / 1175 (0.09%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Upper limb fracture | | | |
| subjects affected / exposed | 1 / 1177 (0.08%) | 0 / 1175 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lower limb fracture | | | |
| subjects affected / exposed | 0 / 1177 (0.00%) | 0 / 1175 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hip fracture | | | |
| subjects affected / exposed | 0 / 1177 (0.00%) | 1 / 1175 (0.09%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|------------------|------------------|---------------|
| Cardiac disorders | | | |
| Myocardial infarction | | | |
| subjects affected / exposed | 1 / 1177 (0.08%) | 4 / 1175 (0.34%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 4 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Coronary artery embolism | | | |
| subjects affected / exposed | 0 / 1177 (0.00%) | 1 / 1175 (0.09%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac arrest | | | |
| subjects affected / exposed | 1 / 1177 (0.08%) | 1 / 1175 (0.09%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Nervous system disorders | | | |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 2 / 1177 (0.17%) | 0 / 1175 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Encephalopathy | | | |
| subjects affected / exposed | 0 / 1177 (0.00%) | 1 / 1175 (0.09%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dizziness | | | |
| subjects affected / exposed | 1 / 1177 (0.08%) | 0 / 1175 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Radial nerve palsy | | | |
| subjects affected / exposed | 0 / 1177 (0.00%) | 1 / 1175 (0.09%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatic encephalopathy | | | |
| subjects affected / exposed | 1 / 1177 (0.08%) | 0 / 1175 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |

| | | | |
|---|------------------|------------------|---------------|
| Ischaemic stroke | | | |
| subjects affected / exposed | 0 / 1177 (0.00%) | 1 / 1175 (0.09%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolic encephalopathy | | | |
| subjects affected / exposed | 0 / 1177 (0.00%) | 1 / 1175 (0.09%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ear and labyrinth disorders | | | |
| Vertigo | | | |
| subjects affected / exposed | 0 / 1177 (0.00%) | 1 / 1175 (0.09%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 1177 (0.00%) | 1 / 1175 (0.09%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 1 / 1177 (0.08%) | 0 / 1175 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colitis | | | |
| subjects affected / exposed | 0 / 1177 (0.00%) | 1 / 1175 (0.09%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Duodenal ulcer perforation | | | |
| subjects affected / exposed | 1 / 1177 (0.08%) | 0 / 1175 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Small intestinal obstruction | | | |
| subjects affected / exposed | 0 / 1177 (0.00%) | 1 / 1175 (0.09%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|------------------|------------------|---------------|
| Oral mucosa erosion | | | |
| subjects affected / exposed | 1 / 1177 (0.08%) | 0 / 1175 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Jejunal perforation | | | |
| subjects affected / exposed | 0 / 1177 (0.00%) | 0 / 1175 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Inguinal hernia | | | |
| subjects affected / exposed | 1 / 1177 (0.08%) | 0 / 1175 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Subcapsular hepatic haematoma | | | |
| subjects affected / exposed | 1 / 1177 (0.08%) | 0 / 1175 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatic necrosis | | | |
| subjects affected / exposed | 1 / 1177 (0.08%) | 0 / 1175 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatic cirrhosis | | | |
| subjects affected / exposed | 1 / 1177 (0.08%) | 0 / 1175 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 0 / 1177 (0.00%) | 1 / 1175 (0.09%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nephrolithiasis | | | |
| subjects affected / exposed | 1 / 1177 (0.08%) | 1 / 1175 (0.09%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|------------------|------------------|---------------|
| Musculoskeletal and connective tissue disorders | | | |
| Lumbar spinal stenosis | | | |
| subjects affected / exposed | 0 / 1177 (0.00%) | 1 / 1175 (0.09%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteoarthritis | | | |
| subjects affected / exposed | 1 / 1177 (0.08%) | 0 / 1175 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Abdominal abscess | | | |
| subjects affected / exposed | 0 / 1177 (0.00%) | 1 / 1175 (0.09%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Abdominal wall abscess | | | |
| subjects affected / exposed | 1 / 1177 (0.08%) | 0 / 1175 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Appendicitis | | | |
| subjects affected / exposed | 1 / 1177 (0.08%) | 0 / 1175 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 1177 (0.00%) | 0 / 1175 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 1177 (0.00%) | 1 / 1175 (0.09%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 1177 (0.00%) | 1 / 1175 (0.09%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|------------------|------------------|---------------|
| Encephalitis viral | | | |
| subjects affected / exposed | 0 / 1177 (0.00%) | 1 / 1175 (0.09%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diverticulitis | | | |
| subjects affected / exposed | 1 / 1177 (0.08%) | 0 / 1175 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peritonitis | | | |
| subjects affected / exposed | 1 / 1177 (0.08%) | 0 / 1175 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia aspiration | | | |
| subjects affected / exposed | 1 / 1177 (0.08%) | 0 / 1175 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sepsis | | | |
| subjects affected / exposed | 2 / 1177 (0.17%) | 0 / 1175 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Tooth abscess | | | |
| subjects affected / exposed | 0 / 1177 (0.00%) | 0 / 1175 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Septic shock | | | |
| subjects affected / exposed | 1 / 1177 (0.08%) | 0 / 1175 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Diabetes mellitus inadequate control | | | |
| subjects affected / exposed | 1 / 1177 (0.08%) | 0 / 1175 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyponatraemia | | | |

| | | | |
|---|------------------|------------------|---------------|
| subjects affected / exposed | 1 / 1177 (0.08%) | 0 / 1175 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | Cohort 2: PCV20 | Cohort 2: V116 | |
|---|-----------------|-----------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 3 / 100 (3.00%) | 1 / 200 (0.50%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Rectal adenocarcinoma | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 200 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Prostate cancer | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 200 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Invasive ductal breast carcinoma | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 200 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 200 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Immune system disorders | | | |
| Drug hypersensitivity | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 200 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute respiratory failure | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 200 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 200 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| Alcohol withdrawal syndrome | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 200 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Alcoholism | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 200 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Delirium tremens | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 200 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Product issues | | | |
| Device occlusion | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 200 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Brain contusion | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 200 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper limb fracture | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 200 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|-----------------|-----------------|--|
| Lower limb fracture | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | 0 / 200 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hip fracture | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 200 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Myocardial infarction | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 200 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Coronary artery embolism | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 200 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac arrest | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 200 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 200 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Encephalopathy | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 200 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dizziness | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 200 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|-----------------|-----------------|--|
| Radial nerve palsy | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 200 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatic encephalopathy | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 200 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ischaemic stroke | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 200 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolic encephalopathy | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 200 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ear and labyrinth disorders | | | |
| Vertigo | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 200 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 200 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 200 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colitis | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 200 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|-----------------|-----------------|--|
| Duodenal ulcer perforation | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 200 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Small intestinal obstruction | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 200 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oral mucosa erosion | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 200 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Jejunal perforation | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | 0 / 200 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Inguinal hernia | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 200 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Subcapsular hepatic haematoma | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 200 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatic necrosis | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 200 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatic cirrhosis | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 200 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |

| | | | |
|---|-----------------|-----------------|--|
| Acute kidney injury | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 200 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nephrolithiasis | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 200 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Lumbar spinal stenosis | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 200 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteoarthritis | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 200 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Abdominal abscess | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 200 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abdominal wall abscess | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 200 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 200 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cellulitis | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | 0 / 200 (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 | 0 / 100 (0.00%) | 0 / 200 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 200 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Encephalitis viral | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 200 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diverticulitis | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 200 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peritonitis | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 200 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia aspiration | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 200 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sepsis | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 200 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tooth abscess | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 1 / 200 (0.50%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Septic shock | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 200 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Diabetes mellitus inadequate control | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 200 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyponatraemia | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 200 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | Cohort 1: V116 | Cohort 1: PCV20 | Unplanned Participants |
|---|---------------------|---------------------|------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 615 / 1177 (52.25%) | 722 / 1175 (61.45%) | 0 / 2 (0.00%) |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 162 / 1177 (13.76%) | 174 / 1175 (14.81%) | 0 / 2 (0.00%) |
| occurrences (all) | 176 | 184 | 0 |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 240 / 1177 (20.39%) | 235 / 1175 (20.00%) | 0 / 2 (0.00%) |
| occurrences (all) | 243 | 237 | 0 |
| Injection site erythema | | | |
| subjects affected / exposed | 82 / 1177 (6.97%) | 86 / 1175 (7.32%) | 0 / 2 (0.00%) |
| occurrences (all) | 83 | 87 | 0 |
| Injection site pain | | | |
| subjects affected / exposed | 471 / 1177 (40.02%) | 608 / 1175 (51.74%) | 0 / 2 (0.00%) |
| occurrences (all) | 474 | 615 | 0 |
| Injection site swelling | | | |

| | | | |
|---|-------------------|--------------------|---------------|
| subjects affected / exposed | 79 / 1177 (6.71%) | 103 / 1175 (8.77%) | 0 / 2 (0.00%) |
| occurrences (all) | 79 | 105 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Myalgia | | | |
| subjects affected / exposed | 75 / 1177 (6.37%) | 82 / 1175 (6.98%) | 0 / 2 (0.00%) |
| occurrences (all) | 75 | 83 | 0 |

| Non-serious adverse events | Cohort 2: PCV20 | Cohort 2: V116 | |
|---|-------------------|--------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 78 / 100 (78.00%) | 161 / 200 (80.50%) | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 26 / 100 (26.00%) | 59 / 200 (29.50%) | |
| occurrences (all) | 29 | 62 | |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 34 / 100 (34.00%) | 81 / 200 (40.50%) | |
| occurrences (all) | 34 | 81 | |
| Injection site erythema | | | |
| subjects affected / exposed | 13 / 100 (13.00%) | 32 / 200 (16.00%) | |
| occurrences (all) | 13 | 32 | |
| Injection site pain | | | |
| subjects affected / exposed | 74 / 100 (74.00%) | 143 / 200 (71.50%) | |
| occurrences (all) | 74 | 143 | |
| Injection site swelling | | | |
| subjects affected / exposed | 14 / 100 (14.00%) | 28 / 200 (14.00%) | |
| occurrences (all) | 14 | 28 | |
| Musculoskeletal and connective tissue disorders | | | |
| Myalgia | | | |
| subjects affected / exposed | 14 / 100 (14.00%) | 33 / 200 (16.50%) | |
| occurrences (all) | 14 | 33 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------|--|
| 16 May 2023 | Amendment 2: Revised the superiority success criterion for serotype 15C. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported