# Clinical trial results:
# A Phase 3, Single-arm Trial to Evaluate the Safety and Immunogenicity of a 20-Valent Pneumococcal Conjugate Vaccine in Healthy Children 15 Months Through 17 Years of Age

## Summary

| | |
|---|---|
| EudraCT number | 2019-003308-11 |
| Trial protocol | Outside EU/EEA |
| Global end of trial date | 06 April 2022 |

### Results information

| | |
|---|---|
| Result version number | v1 |
| This version publication date | 24 September 2022 |
| First version publication date | 24 September 2022 |

## Trial information

### Trial identification

| | |
|---|---|
| Sponsor protocol code | B7471014 |

### Additional study identifiers

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT04642079 |
| WHO universal trial number (UTN) | - |

Notes:

### Sponsors

| | |
|---|---|
| Sponsor organisation name | Pfizer Inc. |
| Sponsor organisation address | 235 E 42nd Street, New York, United States, NY 10017 |
| Public contact | Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com |
| Scientific contact | Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com |

Notes:

### Paediatric regulatory details

| | |
|---|---|
| Is trial part of an agreed paediatric investigation plan (PIP) | Yes |
| EMA paediatric investigation plan number(s) | EMEA-002330-PIP01-18 |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | Yes |

Notes:

## Results analysis stage

| | |
|---|---|
| Analysis stage | Final |
| Date of interim/final analysis | 07 July 2022 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 06 April 2022 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

To describe the safety profile of 20-valent pneumococcal conjugate (20vPnC).
Cohort 1 (subjects aged >=15 to <24 months) and Cohort 2 (subjects aged >=2 to <5 years): To demonstrate that the serotype-specific immunoglobulin G (IgG) concentrations for the 7 additional serotypes 1 month after 20-valent pneumococcal conjugate (20vPnC) are superior to the corresponding IgG concentrations before 20vPnC.
Cohort 3 (subjects aged >=5 to <10 years) and Cohort 4 (subjects aged >=10 to <18 years): To demonstrate that the serotype-specific opsonophagocytic activity (OPA) titers for the 7 additional serotypes 1 month after 20vPnC are superior to the corresponding OPA titers before 20vPnC.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Council for Harmonisation (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 04 December 2020 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | United States: 839 |
| Worldwide total number of subjects | 839 |
| EEA total number of subjects | 0 |

Notes:

### Subjects enrolled per age group

| | |
|---|---|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 210 |
| Children (2-11 years) | 473 |
| Adolescents (12-17 years) | 156 |

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

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

A total of 839 subjects were enrolled and assigned to receive a single dose of 20vPnC of which 8 subjects were not vaccinated and 831 were vaccinated with 20vPnC.

### Period 1

| | |
|---|---|
| Period 1 title | Overall Study (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Cohort 1: 20vPnC: >=15 to <24 Months |

Arm description:

Subjects aged >=15 months to <24 months who have been previously vaccinated with at least 3 doses of 13vPnC, were administered a single dose of 0.5 millilitre (mL) 20vPnC intramuscularly on Day 1.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | 20-Valent Pneumococcal Conjugate Vaccine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Subjects were administered  a single 0.5 mL dose of 20vPnC intramuscularly on Day 1.

| | |
|---|---|
| **Arm title** | Cohort 2: 20vPnC: >=2 to <5 Years |

Arm description:

Subjects aged >=2 to <5 years who have been previously vaccinated with at least 3 doses of 13vPnC, were administered a single dose of  0.5 mL 20vPnC intramuscularly on Day 1.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | 20-Valent Pneumococcal Conjugate Vaccine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Subjects were administered a single 0.5 mL dose of 20vPnC intramuscularly on Day 1.

| | |
|---|---|
| **Arm title** | Cohort 3: 20vPnC: >=5 to <10 Years |

Arm description:

Subjects aged >=5 to <10 years regardless of previous vaccination status with 7vPnC or 13vPnC, were administered a single dose of 0.5 mL 20vPnC intramuscularly into the left arm on Day 1.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | 20-Valent Pneumococcal Conjugate Vaccine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Subjects were administered a single 0.5 mL dose of 20vPnC intramuscularly on Day 1.

| **Arm title** | Cohort 4: 20vPnC: >=10 to <18 Years |
|---|---|

Arm description:

Subjects aged >=10 to <18 years regardless of previous vaccination status with 7vPnC or 13vPnC, were administered a single dose of 0.5 mL 20vPnC intramuscularly into the left arm on Day 1.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | 20-Valent Pneumococcal Conjugate Vaccine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Subjects were administered a single 0.5 mL dose of 20vPnC intramuscularly on Day 1.

| **Number of subjects in period 1** | Cohort 1: 20vPnC: >=15 to <24 Months | Cohort 2: 20vPnC: >=2 to <5 Years | Cohort 3: 20vPnC: >=5 to <10 Years |
|---|---|---|---|
| Started | 210 | 219 | 203 |
| Vaccinated | 209 | 216 | 201 |
| Completed | 207 | 210 | 199 |
| Not completed | 3 | 9 | 4 |
| No longer meets eligibility criteria | 1 | - | 1 |
| Not specified | - | - | - |
| Lost to follow-up | 2 | 5 | 2 |
| Consent withdrawn by parent/guardian/subject | - | 4 | 1 |

| **Number of subjects in period 1** | Cohort 4: 20vPnC: >=10 to <18 Years |
|---|---|
| Started | 207 |
| Vaccinated | 205 |
| Completed | 203 |
| Not completed | 4 |
| No longer meets eligibility criteria | 1 |
| Not specified | 1 |
| Lost to follow-up | - |
| Consent withdrawn by parent/guardian/subject | 2 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Cohort 1: 20vPnC: >=15 to <24 Months |
| Reporting group description: | |
| Subjects aged >=15 months to <24 months who have been previously vaccinated with at least 3 doses of 13vPnC, were administered a single dose of 0.5 millilitre (mL) 20vPnC intramuscularly on Day 1. | |
| Reporting group title | Cohort 2: 20vPnC: >=2 to <5 Years |
| Reporting group description: | |
| Subjects aged >=2 to <5 years who have been previously vaccinated with at least 3 doses of 13vPnC, were administered a single dose of 0.5 mL 20vPnC intramuscularly on Day 1. | |
| Reporting group title | Cohort 3: 20vPnC: >=5 to <10 Years |
| Reporting group description: | |
| Subjects aged >=5 to <10 years regardless of previous vaccination status with 7vPnC or 13vPnC, were administered a single dose of 0.5 mL 20vPnC intramuscularly into the left arm on Day 1. | |
| Reporting group title | Cohort 4: 20vPnC: >=10 to <18 Years |
| Reporting group description: | |
| Subjects aged >=10 to <18 years regardless of previous vaccination status with 7vPnC or 13vPnC, were administered a single dose of 0.5 mL 20vPnC intramuscularly into the left arm on Day 1. | |

| Reporting group values | Cohort 1: 20vPnC: >=15 to <24 Months | Cohort 2: 20vPnC: >=2 to <5 Years | Cohort 3: 20vPnC: >=5 to <10 Years |
|---|---|---|---|
| Number of subjects | 210 | 219 | 203 |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23months) | 210 | 0 | 0 |
| Children (2-11 years) | 0 | 219 | 203 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 0 | 0 | 0 |
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |
| Age Continuous | | | |
| Age is reported in Months for 'Cohort 1: 20vPnC: >=15 to <24 Months' | | | |
| Units: years | | | |
| arithmetic mean | 18.3 | 3.0 | 7.2 |
| standard deviation | ± 2.67 | ± 0.82 | ± 1.38 |
| Sex: Female, Male | | | |
| Units: Subjects | | | |
| Female | 93 | 111 | 94 |
| Male | 117 | 108 | 109 |
| Race | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 1 | 0 |
| Asian | 3 | 0 | 0 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Black or African American | 26 | 26 | 22 |
| White | 169 | 175 | 176 |
| More than one race | 10 | 14 | 5 |
| Unknown or Not Reported | 2 | 3 | 0 |
| Ethnicity<br>Units: Subjects | | | |
| Hispanic or Latino | 35 | 46 | 32 |
| Not Hispanic or Latino | 173 | 173 | 169 |
| Unknown or Not Reported | 2 | 0 | 2 |

| **Reporting group values** | Cohort 4: 20vPnC: >=10 to <18 Years | Total | |
|---|---|---|---|
| Number of subjects | 207 | 839 | |
| Age categorical<br>Units: Subjects | | | |
| In utero | 0 | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | |
| Newborns (0-27 days) | 0 | 0 | |
| Infants and toddlers (28 days-23months) | 0 | 210 | |
| Children (2-11 years) | 51 | 473 | |
| Adolescents (12-17 years) | 156 | 156 | |
| Adults (18-64 years) | 0 | 0 | |
| From 65-84 years | 0 | 0 | |
| 85 years and over | 0 | 0 | |
| Age Continuous | | | |
| Age is reported in Months for 'Cohort 1: 20vPnC: >=15 to <24 Months' | | | |
| Units: years | | | |
| arithmetic mean | 13.6 | | |
| standard deviation | ± 2.32 | - | |
| Sex: Female, Male<br>Units: Subjects | | | |
| Female | 91 | 389 | |
| Male | 116 | 450 | |
| Race<br>Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 1 | |
| Asian | 0 | 3 | |
| Native Hawaiian or Other Pacific Islander | 1 | 1 | |
| Black or African American | 17 | 91 | |
| White | 180 | 700 | |
| More than one race | 9 | 38 | |
| Unknown or Not Reported | 0 | 5 | |
| Ethnicity<br>Units: Subjects | | | |
| Hispanic or Latino | 45 | 158 | |
| Not Hispanic or Latino | 161 | 676 | |
| Unknown or Not Reported | 1 | 5 | |

## End points

### End points reporting groups

| Reporting group title | Cohort 1: 20vPnC: >=15 to <24 Months |
|---|---|
| Reporting group description: | |
| Subjects aged >=15 months to <24 months who have been previously vaccinated with at least 3 doses of 13vPnC, were administered a single dose of 0.5 millilitre (mL) 20vPnC intramuscularly on Day 1. | |
| Reporting group title | Cohort 2: 20vPnC: >=2 to <5 Years |
| Reporting group description: | |
| Subjects aged >=2 to <5 years who have been previously vaccinated with at least 3 doses of 13vPnC, were administered a single dose of 0.5 mL 20vPnC intramuscularly on Day 1. | |
| Reporting group title | Cohort 3: 20vPnC: >=5 to <10 Years |
| Reporting group description: | |
| Subjects aged >=5 to <10 years regardless of previous vaccination status with 7vPnC or 13vPnC, were administered a single dose of 0.5 mL 20vPnC intramuscularly into the left arm on Day 1. | |
| Reporting group title | Cohort 4: 20vPnC: >=10 to <18 Years |
| Reporting group description: | |
| Subjects aged >=10 to <18 years regardless of previous vaccination status with 7vPnC or 13vPnC, were administered a single dose of 0.5 mL 20vPnC intramuscularly into the left arm on Day 1. | |

### Primary: Percentage of Subjects Reporting Prompted Local Reactions Within 7 Days After Vaccination

| End point title | Percentage of Subjects Reporting Prompted Local Reactions Within 7 Days After Vaccination[1] |
|---|---|
| End point description: | |
| Local reactions included pain at injection site, redness and swelling recorded by parent's/legal guardian's of subjects in an electronic diary (e-diary). Redness and swelling were measured and recorded in measuring device units. One measuring device unit =0.5 centimetre (cm). Redness and swelling were graded as mild: greater than (>) 0.0 to 2.0 cm, moderate: >2.0 to 7.0 cm and severe: >7.0 cm. Pain at injection site was graded as mild: hurt if gently touched (cohort 1) and did not interfere with activity (cohort 2-4); moderate: hurt if gently touched with crying (cohort 1) and interfered with daily activity (cohort 2-4) and; severe: limited limb movement (cohort 1) and prevented daily activity (cohort 2-4). 95 percent (%) confidence interval (CI) was based on Clopper and Pearson method. Safety population included all subjects who received 20vPnC and had safety follow-up after vaccination. Here, "Number of Subjects Analysed" signifies subjects evaluable for this endpoint. | |
| End point type | Primary |
| End point timeframe: | |
| Within 7 days after 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.<br>Justification: No statistical analysis were performed. | |

| End point values | Cohort 1: 20vPnC: >=15 to <24 Months | Cohort 2: 20vPnC: >=2 to <5 Years | Cohort 3: 20vPnC: >=5 to <10 Years | Cohort 4: 20vPnC: >=10 to <18 Years |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 204 | 215 | 199 | 205 |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Redness: Any | 37.7 (31.1 to 44.8) | 39.1 (32.5 to 45.9) | 37.2 (30.5 to 44.3) | 15.1 (10.5 to 20.8) |
| Redness: Mild | 30.4 (24.2 to 37.2) | 22.8 (17.4 to 29.0) | 16.6 (11.7 to 22.5) | 10.7 (6.8 to 15.8) |

| | | | | |
|---|---|---|---|---|
| Redness: Moderate | 7.4 (4.2 to 11.8) | 15.3 (10.8 to 20.9) | 18.6 (13.4 to 24.7) | 3.9 (1.7 to 7.5) |
| Redness: Severe | 0 (0.0 to 1.8) | 0.9 (0.1 to 3.3) | 2.0 (0.6 to 5.1) | 0.5 (0.0 to 2.7) |
| Swelling: Any | 22.1 (16.6 to 28.4) | 23.3 (17.8 to 29.5) | 27.1 (21.1 to 33.9) | 15.6 (10.9 to 21.3) |
| Swelling: Mild | 15.7 (11.0 to 21.4) | 11.6 (7.7 to 16.7) | 10.6 (6.7 to 15.7) | 5.4 (2.7 to 9.4) |
| Swelling: Moderate | 6.4 (3.4 to 10.7) | 11.2 (7.3 to 16.2) | 15.6 (10.8 to 21.4) | 10.2 (6.5 to 15.2) |
| Swelling: Severe | 0 (0.0 to 1.8) | 0.5 (0.0 to 2.6) | 1.0 (0.1 to 3.6) | 0 (0.0 to 1.8) |
| Pain at injection site: Any | 52.5 (45.4 to 59.5) | 66.0 (59.3 to 72.3) | 82.9 (77.0 to 87.9) | 82.0 (76.0 to 87.0) |
| Pain at injection site: Mild | 41.7 (34.8 to 48.8) | 47.0 (40.2 to 53.9) | 56.8 (49.6 to 63.8) | 62.9 (55.9 to 69.6) |
| Pain at the injection site: Moderate | 9.8 (6.1 to 14.7) | 17.7 (12.8 to 23.4) | 24.6 (18.8 to 31.2) | 17.6 (12.6 to 23.5) |
| Pain at the injection site: Severe | 1.0 (0.1 to 3.5) | 1.4 (0.3 to 4.0) | 1.5 (0.3 to 4.3) | 1.5 (0.3 to 4.2) |

## Statistical analyses

No statistical analyses for this end point

## Primary: Percentage of Subjects Reporting Prompted Systemic Events Within 7 Days After Vaccination: Cohort 1

| End point title | Percentage of Subjects Reporting Prompted Systemic Events Within 7 Days After Vaccination: Cohort 1[2][3] |
|---|---|

End point description:

Systemic events for Cohort 1 were recorded by parents/legal guardians of subject's using an e-diary. Fever was defined as temperature greater than or equal to (>=) 38.0 degree Celsius (C) and categorised as >=38.0 to 38.4 degree C, >38.4 to 38.9 degree C, >38.9 to 40.0 degree C and >40.0 degree C. Decreased appetite was graded as mild (decreased interest in eating), moderate (decreased oral intake) and severe (refusal to feed). Drowsiness was graded as mild (increased or prolonged sleeping bouts), moderate (slightly subdued, interfered with daily activity) and severe (disabling, not interested in usual daily activity). Irritability: graded as mild (easily consolable), moderate (required increased attention) and severe (inconsolable, crying could not be comforted). 95% CI was based on Clopper and Pearson method. Safety population included all subjects who received 20vPnC and had safety follow-up after vaccination. "Number of Subjects Analysed" = subjects evaluable for this endpoint.

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

End point timeframe:

Within 7 days after vaccination

Notes:

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

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analysed only for the specified reporting arms.

| **End point values** | Cohort 1: 20vPnC: >=15 to <24 Months | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 204 | | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |

| | | | | |
|---|---|---|---|---|
| Fever: =>38.0 degree C | 11.8 (7.7 to 17.0) | | | |
| Fever: =>38.0 degree C to 38.4 degree C | 5.9 (3.1 to 10.0) | | | |
| Fever: >38.4 degree C to 38.9 degree C | 2.9 (1.1 to 6.3) | | | |
| Fever: >38.9 degree C to 40.0 degree C | 2.9 (1.1 to 6.3) | | | |
| Fever: >40.0 degree C | 0 (0.0 to 1.8) | | | |
| Decreased appetite: Any | 25.0 (19.2 to 31.5) | | | |
| Decreased appetite: Mild | 17.6 (12.7 to 23.6) | | | |
| Decreased appetite: Moderate | 6.4 (3.4 to 10.7) | | | |
| Decreased appetite: Severe | 1.0 (0.1 to 3.5) | | | |
| Drowsiness/increased sleep: Any | 41.7 (34.8 to 48.8) | | | |
| Drowsiness/increased sleep: Mild | 31.4 (25.1 to 38.2) | | | |
| Drowsiness/increased sleep: Moderate | 9.3 (5.7 to 14.2) | | | |
| Drowsiness/increased sleep: Severe | 1.0 (0.1 to 3.5) | | | |
| Irritability: Any | 61.8 (54.7 to 68.5) | | | |
| Irritability: Mild | 22.5 (17.0 to 28.9) | | | |
| Irritability: Moderate | 37.3 (30.6 to 44.3) | | | |
| Irritability: Severe | 2.0 (0.5 to 4.9) | | | |

## Statistical analyses

No statistical analyses for this end point

## Primary: Percentage of Subjects Reporting Prompted Systemic Events Within 7 Days After Vaccination: Cohorts 2, 3 and 4

| End point title | Percentage of Subjects Reporting Prompted Systemic Events Within 7 Days After Vaccination: Cohorts 2, 3 and 4[4][5] |
|---|---|

End point description:

Systemic events for Cohort 2-4 included fever, fatigue, headache, muscle pain and joint pain, recorded by parents/legal guardians of subject's using an e-diary. Fever was defined as temperature >=38.0 degree C and categorised as >=38.0 to 38.4 degree C,>38.4 to 38.9 degree C,>38.9 to 40.0 degree C and >40.0 degree C. Fatigue, headache, muscle pain and joint pain were graded as mild (no interference with activity), moderate (some interference with activity) and severe (prevents daily routine activity). 95% CI was based on Clopper and Pearson method. Safety population included all subjects who received 20vPnC and had safety follow-up after vaccination. "Number of Subjects Analysed" = subjects evaluable for this endpoint.

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

End point timeframe:

Within 7 days after vaccination

Notes:

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

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analysed only for the specified reporting arms.

| End point values | Cohort 2: 20vPnC: >=2 to <5 Years | Cohort 3: 20vPnC: >=5 to <10 Years | Cohort 4: 20vPnC: >=10 to <18 Years | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 215 | 199 | 205 | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Fever: =>38.0 degree C | 3.3 (1.3 to 6.6) | 0.5 (0.0 to 2.8) | 0 (0.0 to 1.8) | |
| Fever: =>38.0 degree C to 38.4 degree C | 1.4 (0.3 to 4.0) | 0.5 (0.0 to 2.8) | 0 (0.0 to 1.8) | |
| Fever: 38.4 degree C to 38.9 degree C | 1.4 (0.3 to 4.0) | 0 (0.0 to 1.8) | 0 (0.0 to 1.8) | |
| Fever: 38.9 degree C to 40.0 degree C | 0.5 (0.0 to 2.6) | 0 (0.0 to 1.8) | 0 (0.0 to 1.8) | |
| Fever: =>40.0 degree C | 0 (0.0 to 1.7) | 0 (0.0 to 1.8) | 0 (0.0 to 1.8) | |
| Fatigue: Any | 37.2 (30.7 to 44.0) | 28.1 (22.0 to 34.9) | 27.8 (21.8 to 34.5) | |
| Fatigue: Mild | 21.9 (16.5 to 28.0) | 19.1 (13.9 to 25.3) | 15.6 (10.9 to 21.3) | |
| Fatigue: Moderate | 14.4 (10.0 to 19.8) | 8.5 (5.1 to 13.3) | 12.2 (8.0 to 17.5) | |
| Fatigue: Severe | 0.9 (0.1 to 3.3) | 0.5 (0.0 to 2.8) | 0 (0.0 to 1.8) | |
| Headache: Any | 5.6 (2.9 to 9.5) | 18.6 (13.4 to 24.7) | 29.3 (23.1 to 36.0) | |
| Headache: Mild | 3.3 (1.3 to 6.6) | 14.6 (10.0 to 20.3) | 20.0 (14.8 to 26.1) | |
| Headache: Moderate | 1.9 (0.5 to 4.7) | 3.0 (1.1 to 6.4) | 7.8 (4.5 to 12.4) | |
| Headache: Severe | 0.5 (0.0 to 2.6) | 1.0 (0.1 to 3.6) | 1.5 (0.3 to 4.2) | |
| Muscle pain: Any | 26.5 (20.7 to 32.9) | 39.2 (32.4 to 46.3) | 48.3 (41.3 to 55.4) | |
| Muscle pain: Mild | 17.7 (12.8 to 23.4) | 26.6 (20.6 to 33.3) | 34.6 (28.1 to 41.6) | |
| Muscle pain: Moderate | 8.4 (5.0 to 12.9) | 11.1 (7.1 to 16.3) | 13.2 (8.9 to 18.6) | |
| Muscle pain: Severe | 0.5 (0.0 to 2.6) | 1.5 (0.3 to 4.3) | 0.5 (0.0 to 2.7) | |
| Joint pain: Any | 3.7 (1.6 to 7.2) | 6.5 (3.5 to 10.9) | 8.3 (4.9 to 12.9) | |
| Joint pain: Mild | 2.3 (0.8 to 5.3) | 3.0 (1.1 to 6.4) | 3.4 (1.4 to 6.9) | |
| Joint pain: Moderate | 1.4 (0.3 to 4.0) | 3.0 (1.1 to 6.4) | 4.9 (2.4 to 8.8) | |
| Joint pain: Severe | 0 (0.0 to 1.7) | 0.5 (0.0 to 2.8) | 0 (0.0 to 1.8) | |

### Statistical analyses

No statistical analyses for this end point

## Primary: Percentage of Subjects Reporting Adverse Events (AEs) up to 1 Month After Vaccination

| End point title | Percentage of Subjects Reporting Adverse Events (AEs) up to 1 Month After Vaccination[6] |
|---|---|

End point description:

An AE was any untoward medical occurrence in a subject, temporally associated with the use of study treatment, whether or not considered related to the study treatment. 95% CI was based on the Clopper and Pearson method. Safety population included all subjects who received 20vPnC and had safety follow-up after vaccination.

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

End point timeframe:

From Day 1 of vaccination up to 1 month after vaccination

Notes:

[6] - 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 analysis were performed.

| **End point values** | Cohort 1: 20vPnC: >=15 to <24 Months | Cohort 2: 20vPnC: >=2 to <5 Years | Cohort 3: 20vPnC: >=5 to <10 Years | Cohort 4: 20vPnC: >=10 to <18 Years |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 209 | 216 | 201 | 205 |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | 23.9 (18.3 to 30.3) | 7.9 (4.7 to 12.3) | 6.5 (3.5 to 10.8) | 4.4 (2.0 to 8.2) |

## Statistical analyses

No statistical analyses for this end point

## Primary: Percentage of Subjects Reporting Serious Adverse Events (SAEs) up to 6 Months After Vaccination

| End point title | Percentage of Subjects Reporting Serious Adverse Events (SAEs) up to 6 Months After Vaccination[7] |
|---|---|

End point description:

An SAE was any untoward medical occurrence that occurred, at any dose: resulted in death; required inpatient hospitalisation or prolongation of existing hospitalisation; was life-threatening; resulted in persistent or significant disability/ incapacity; was a congenital anomaly/birth defect and other important medical events. 95% CI was based on the Clopper and Pearson method. Safety population included all subjects who received 20vPnC and had safety follow-up after vaccination.

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

End point timeframe:

From Day 1 of vaccination up to 6 months after vaccination

Notes:

[7] - 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 analysis were performed.

| **End point values** | Cohort 1: 20vPnC: >=15 to <24 Months | Cohort 2: 20vPnC: >=2 to <5 Years | Cohort 3: 20vPnC: >=5 to <10 Years | Cohort 4: 20vPnC: >=10 to <18 Years |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 209 | 216 | 201 | 205 |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | 0.5 (0.0 to 2.6) | 0 (0.0 to 1.7) | 0 (0.0 to 1.8) | 1.5 (0.3 to 4.2) |

## Statistical analyses

No statistical analyses for this end point

## Primary: Percentage of Subjects Reporting Newly Diagnosed Chronic Medical Conditions (NDCMCs) up to 6 Months After Vaccination

| End point title | Percentage of Subjects Reporting Newly Diagnosed Chronic Medical Conditions (NDCMCs) up to 6 Months After Vaccination[8] |
|---|---|

End point description:

An NDCMC was defined as a disease or medical condition, not previously identified, that was expected to be persistent or was otherwise long-lasting in its effects. 95% CI was based on the Clopper and Pearson method. Safety population included all subjects who received 20vPnC and had safety follow-up after vaccination.

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

End point timeframe:

From Day 1 of vaccination up to 6 months after vaccination

Notes:

[8] - 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 analysis were performed.

| End point values | Cohort 1: 20vPnC: >=15 to <24 Months | Cohort 2: 20vPnC: >=2 to <5 Years | Cohort 3: 20vPnC: >=5 to <10 Years | Cohort 4: 20vPnC: >=10 to <18 Years |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 209 | 216 | 201 | 205 |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | 1.9 (0.5 to 4.8) | 0.5 (0.0 to 2.6) | 0.5 (0.0 to 2.7) | 1.0 (0.1 to 3.5) |

### Statistical analyses

No statistical analyses for this end point

## Primary: Geometric Mean Fold Rises (GMFRs) of Pneumococcal Serotype-Specific Immunoglobulin G (IgG) Concentrations for the 7 Additional Serotypes From Before to 1 Month After 20vPnC Vaccination: Cohort 1 and 2

| End point title | Geometric Mean Fold Rises (GMFRs) of Pneumococcal Serotype-Specific Immunoglobulin G (IgG) Concentrations for the 7 Additional Serotypes From Before to 1 Month After 20vPnC Vaccination: Cohort 1 and 2[9][10] |
|---|---|

End point description:

Pneumococcal serotype-specific IgG concentrations were measured from serum samples for 7 additional 20vPnC serotypes: 8, 10A, 11A, 12F, 15B, 22F and 33F. GMFR=geometric mean of fold rise from before vaccination on Day 1 to 1 month after vaccination with 20vPnC. GMFRs and corresponding 2-sided CIs were calculated by exponentiating the mean logarithm of titres or fold rises and the corresponding CIs (based on Student t distribution). Superiority of IgG concentration 1 month after 20vPnC to before vaccination for each serotype was demonstrated if the 95% lower CI of GMFR was >1. Evaluable immunogenicity population (EIP) included all subjects who were eligible; received 20vPnC; at least 1 valid immunogenicity result from 1 month after vaccination collected within 27 to 56 days after vaccination for Cohorts 1-2; no other major protocol deviations. Number of Subjects Analysed=subjects included in the EIP and n=subjects with valid assay results at both timepoints for the specified serotype.

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

End point timeframe:

Before vaccination to 1 month after vaccination

Notes:

[9] - 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 analysis were performed.

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analysed only for the specified reporting arms.

| **End point values** | Cohort 1: 20vPnC: >=15 to <24 Months | Cohort 2: 20vPnC: >=2 to <5 Years | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 190 | 183 | | |
| Units: Fold rise | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Serotype 8 (n=186, 178) | 113.4 (93.2 to 137.9) | 107.0 (86.1 to 133.0) | | |
| Serotype 10A (n=188, 181) | 83.2 (69.1 to 100.2) | 106.7 (86.2 to 132.0) | | |
| Serotype 11A (n=188, 182) | 62.6 (49.8 to 78.6) | 43.5 (33.2 to 57.1) | | |
| Serotype 12F (n=188, 182) | 27.9 (22.9 to 34.1) | 36.6 (30.1 to 44.7) | | |
| Serotype 15B (n=188, 180) | 52.1 (43.2 to 62.8) | 73.3 (58.7 to 91.5) | | |
| Serotype 22F (n=188, 182) | 1847.7 (1481.3 to 2304.5) | 796.2 (577.1 to 1098.4) | | |
| Serotype 33F (n=188, 182) | 113.5 (92.5 to 139.2) | 78.3 (61.6 to 99.5) | | |

### Statistical analyses

No statistical analyses for this end point

## Primary: GMFRs of Pneumococcal Serotype-Specific Opsonophagocytic Activity (OPA) Titres for the 7 Additional Serotypes From Before to 1 Month After 20PnC Vaccination: Cohort 3 and 4

| End point title | GMFRs of Pneumococcal Serotype-Specific Opsonophagocytic Activity (OPA) Titres for the 7 Additional Serotypes From Before to 1 Month After 20PnC Vaccination: Cohort 3 and 4[11][12] |
|---|---|

End point description:

Pneumococcal serotype-specific OPA titers were measured from serum samples for 7 additional 20vPnC serotypes: 8, 10A, 11A, 12F, 15B, 22F and 33F. GMFR was calculated as geometric mean of fold rise from before vaccination on Day 1 to 1 month after vaccination with 20vPnC. GMFRs and the corresponding 2-sided CIs were calculated by exponentiating the mean logarithm of the titres or fold rises and the corresponding CIs (based on the Student t distribution). Superiority of OPA titers 1 month after 20vPnC to before vaccination for each serotype was demonstrated if the 95% lower CI of the GMFR was >1. EIP included all subjects who were eligible; received 20vPnC; at least 1 valid immunogenicity result from 1 month after vaccination collected within 27 to 49 days after vaccination for Cohorts 3-4; no other major protocol deviations. Here, Number of Subjects Analysed=subjects included in the EIP and n=subjects with valid assay results at both timepoints for the specified serotype.

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

End point timeframe:

Before vaccination to 1 month after vaccination

Notes:

[11] - 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 analysis were performed.

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analysed only for the specified reporting arms.

| **End point values** | Cohort 3: 20vPnC: >=5 to <10 Years | Cohort 4: 20vPnC: >=10 to <18 Years | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 186 | 198 | | |
| Units: Fold rise | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Serotype 8 (n=153, 174) | 106.5 (79.9 to 142.0) | 86.3 (64.2 to 115.9) | | |
| Serotype 10A (n=134, 142) | 30.6 (20.1 to 46.6) | 33.5 (22.3 to 50.1) | | |
| Serotype 11A (n=136, 155) | 11.6 (7.6 to 17.7) | 14.9 (10.2 to 21.8) | | |
| Serotype 12F (n=154, 164) | 463.6 (332.3 to 646.7) | 454.1 (333.3 to 618.7) | | |
| Serotype 15B (n=142, 164) | 380.8 (228.3 to 635.2) | 499.0 (338.7 to 735.3) | | |
| Serotype 22F (n=137, 168) | 128.5 (76.7 to 215.3) | 111.2 (67.1 to 184.3) | | |
| Serotype 33F (n=144, 158) | 14.2 (10.9 to 18.4) | 11.5 (8.9 to 14.9) | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Subjects With Predefined Levels of Pneumococcal Serotype-Specific IgG Concentrations for the 7 Additional Serotypes at 1 Month After Vaccination in Cohort 1 Only

| End point title | Percentage of Subjects With Predefined Levels of Pneumococcal Serotype-Specific IgG Concentrations for the 7 Additional Serotypes at 1 Month After Vaccination in Cohort 1 Only[13] |
|---|---|

End point description:

Pneumococcal serotype-specific IgG concentrations were measured from serum samples for 7 additional 20vPnC serotypes: 8, 10A, 11A, 12F, 15B, 22F and 33F. Percentage of subjects with predefined level (>=0.35 micrograms per millilitre (mcg/mL) of IgG concentration for the 7 additional 20vPnC serotypes was presented. 95% CI was based on Clopper and Pearson method. EIP included all subjects who were eligible; received 20vPnC; at least 1 valid immunogenicity result from 1 month after vaccination collected within 27 to 56 days after vaccination for Cohort 1; no other major protocol deviations. Here, "Number of Subjects Analysed" signifies subjects included in the EIP with valid assay results.

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

End point timeframe:

At 1 Month after vaccination

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analysed only for the specified reporting arms.

| End point values | Cohort 1: 20vPnC: >=15 to <24 Months | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 190 | | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Serotype 8 | 100.0 (98.1 to 100.0) | | | |
| Serotype 10A | 83.2 (77.1 to 88.2) | | | |
| Serotype 11A | 93.2 (88.6 to 96.3) | | | |
| Serotype 12F | 40.0 (33.0 to 47.3) | | | |
| Serotype 15B | 83.7 (77.6 to 88.6) | | | |
| Serotype 22F | 98.9 (96.2 to 99.9) | | | |
| Serotype 33F | 92.6 (87.9 to 95.9) | | | |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Geometric Mean Concentrations (GMCs) of Pneumococcal Serotype-Specific IgG for the 20vPnC Serotypes Before and 1 Month After Vaccination**

| End point title | Geometric Mean Concentrations (GMCs) of Pneumococcal Serotype-Specific IgG for the 20vPnC Serotypes Before and 1 Month After Vaccination |
|---|---|

End point description:

Pneumococcal serotype-specific IgG concentrations were measured for serum samples for 13vPnC serotypes: 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F; and 7 additional 20vPnC serotypes: 8, 10A, 11A, 12F, 15B, 22F and 33F. GMCs were calculated by exponentiating the mean logarithm of the concentrations and the corresponding CIs (based on the Student t distribution). EIP included all subjects who were eligible; received 20vPnC; at least 1 valid immunogenicity result from 1 month after vaccination collected within 27 to 56 days or within 27 to 49 days after vaccination for Cohorts 1-2 or Cohorts 3-4, respectively; no other major protocol deviations. Here, "Number of Subjects Analysed" signifies subjects included in the EIP and n=subjects with valid IgG concentrations at the specified timepoint.

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

End point timeframe:

Before vaccination (Vacc.) and 1 month after vaccination (1M after Vacc.)

| End point values | Cohort 1: 20vPnC: >=15 to <24 Months | Cohort 2: 20vPnC: >=2 to <5 Years | Cohort 3: 20vPnC: >=5 to <10 Years | Cohort 4: 20vPnC: >=10 to <18 Years |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 190 | 183 | 186 | 198 |
| Units: Micrograms per millilitre | | | | |
| geometric mean (confidence interval 95%) | | | | |

| | | | | |
|---|---|---|---|---|
| Before Vacc.,Serotype 1 (n=189,183,186,198) | 0.43 (0.37 to 0.49) | 0.20 (0.17 to 0.24) | 0.12 (0.10 to 0.14) | 0.09 (0.08 to 0.11) |
| 1M after Vacc.,Serotype 1 (n=190,183,186,198) | 1.46 (1.28 to 1.67) | 4.21 (3.62 to 4.90) | 5.86 (5.15 to 6.67) | 4.04 (3.32 to 4.93) |
| Before Vacc.,Serotype 3 (n=189,183,186,198) | 0.14 (0.12 to 0.16) | 0.08 (0.06 to 0.10) | 0.22 (0.17 to 0.30) | 0.15 (0.11 to 0.20) |
| 1M after Vacc.,Serotype 3 (n=190,183,186,198) | 0.54 (0.47 to 0.61) | 1.21 (1.04 to 1.42) | 1.32 (1.16 to 1.50) | 0.62 (0.52 to 0.76) |
| Before Vacc.,Serotype 4 (n=189,183,186,198) | 0.61 (0.52 to 0.72) | 0.30 (0.25 to 0.37) | 0.13 (0.11 to 0.16) | 0.12 (0.10 to 0.15) |
| 1M after Vacc.,Serotype 4 (n=190, 183, 186, 198) | 2.59 (2.27 to 2.96) | 8.37 (7.28 to 9.62) | 9.76 (8.54 to 11.15) | 6.37 (5.39 to 7.53) |
| Before Vacc.,Serotype 5 (n=189,183,186,198) | 0.43 (0.36 to 0.50) | 0.18 (0.15 to 0.22) | 0.07 (0.06 to 0.08) | 0.04 (0.03 to 0.06) |
| 1M after Vacc.,Serotype 5 (n=190,183,186,198) | 1.53 (1.32 to 1.77) | 5.09 (4.32 to 5.99) | 7.50 (6.52 to 8.63) | 2.58 (1.88 to 3.53) |
| Before Vacc.,Serotype 6A (n=188,183,184,195) | 1.61 (1.38 to 1.88) | 0.71 (0.58 to 0.88) | 0.50 (0.39 to 0.65) | 0.28 (0.22 to 0.37) |
| 1M after Vacc.,Serotype 6A (n=190,183,186,198) | 7.59 (6.67 to 8.63) | 31.99 (27.85 to 36.75) | 46.28 (39.90 to 53.67) | 20.03 (15.39 to 26.07) |
| Before Vacc.,Serotype 6B (n=188,183,182,195) | 0.85 (0.71 to 1.02) | 0.52 (0.42 to 0.63) | 0.26 (0.20 to 0.32) | 0.40 (0.31 to 0.51) |
| 1M after Vacc.,Serotype 6B (n=190,183,186,198) | 4.27 (3.69 to 4.94) | 17.78 (15.43 to 20.48) | 32.45 (27.90 to 37.74) | 38.82 (31.49 to 47.86) |
| Before Vacc.,Serotype 7F (n=189,183,186,198) | 1.17 (1.03 to 1.33) | 0.51 (0.44 to 0.60) | 0.18 (0.16 to 0.21) | 0.11 (0.08 to 0.14) |
| 1M after Vacc.,Serotype 7F (n=190,183,186,198) | 3.53 (3.16 to 3.94) | 6.42 (5.69 to 7.24) | 7.92 (7.03 to 8.93) | 3.19 (2.65 to 3.85) |
| Before Vacc.,Serotype 9V (n=189,183,186,198) | 0.71 (0.61 to 0.83) | 0.35 (0.28 to 0.42) | 0.14 (0.11 to 0.17) | 0.14 (0.11 to 0.18) |
| 1M after Vacc.,Serotype 9V (n=190,183,186,198) | 2.70 (2.35 to 3.09) | 7.94 (6.83 to 9.24) | 10.86 (9.41 to 12.54) | 7.67 (6.52 to 9.02) |
| Before Vacc.,Serotype 14 (n=188,183,186,198) | 1.53 (1.31 to 1.79) | 0.66 (0.53 to 0.81) | 0.42 (0.33 to 0.53) | 0.29 (0.23 to 0.37) |
| 1M after Vacc.,Serotype 14 (n=189,183,186,198) | 4.42 (3.82 to 5.12) | 14.60 (12.44 to 17.13) | 28.54 (24.77 to 32.89) | 28.17 (23.90 to 33.21) |
| Before Vacc.,Serotype 18C (n=189,183,186,198) | 0.65 (0.55 to 0.76) | 0.26 (0.21 to 0.32) | 0.12 (0.09 to 0.14) | 0.13 (0.11 to 0.17) |
| 1M after Vacc.,Serotype 18C (n=190,183,186,198) | 2.69 (2.32 to 3.12) | 7.07 (6.01 to 8.32) | 10.83 (9.53 to 12.30) | 8.61 (7.34 to 10.10) |
| Before Vacc.,Serotype 19A (n=189,183,186,198) | 0.47 (0.38 to 0.58) | 0.52 (0.40 to 0.68) | 0.78 (0.58 to 1.04) | 0.55 (0.43 to 0.70) |
| 1M after Vacc.,Serotype 19A (n=189,183,186,197) | 3.29 (2.89 to 3.76) | 12.48 (10.76 to 14.48) | 13.65 (11.96 to 15.59) | 8.89 (7.29 to 10.84) |
| Before Vacc.,Serotype 19F (n=189,183,186,198) | 0.80 (0.67 to 0.94) | 0.56 (0.44 to 0.71) | 0.96 (0.70 to 1.32) | 0.82 (0.63 to 1.06) |
| 1M after Vacc.,Serotype 19F (n=190,183,186,198) | 4.16 (3.61 to 4.79) | 12.50 (10.48 to 14.91) | 14.62 (12.32 to 17.36) | 6.55 (5.60 to 7.66) |
| Before Vacc.,Serotype 23F (n=189,183,186,198) | 0.96 (0.79 to 1.18) | 0.90 (0.71 to 1.15) | 0.82 (0.64 to 1.06) | 0.61 (0.48 to 0.78) |
| 1M after Vacc.,Serotype 23F (n=190,183,186,198) | 5.35 (4.55 to 6.30) | 16.18 (13.75 to 19.04) | 22.69 (19.40 to 26.53) | 19.16 (16.31 to 22.51) |
| Before Vacc.,Serotype 8 (n=186,179,185,196) | 0.04 (0.03 to 0.05) | 0.05 (0.04 to 0.06) | 0.08 (0.07 to 0.10) | 0.16 (0.12 to 0.20) |
| 1M after Vacc.,Serotype 8 (n=190,182,186,198) | 4.66 (4.17 to 5.22) | 5.08 (4.45 to 5.80) | 4.65 (4.05 to 5.34) | 4.26 (3.67 to 4.94) |
| Before Vacc.,Serotype 10A (n=188,183,186,198) | 0.01 (0.01 to 0.02) | 0.03 (0.02 to 0.03) | 0.07 (0.06 to 0.09) | 0.15 (0.12 to 0.19) |
| 1M after Vacc.,Serotype 10A (n=190,181,186,198) | 1.23 (1.02 to 1.48) | 2.76 (2.28 to 3.34) | 3.98 (3.25 to 4.88) | 5.35 (4.20 to 6.81) |
| Before Vacc.,Serotype 11A (n=188,183,186,198) | 0.03 (0.02 to 0.03) | 0.06 (0.04 to 0.08) | 0.12 (0.09 to 0.16) | 0.30 (0.23 to 0.38) |

| | | | | |
|---|---|---|---|---|
| 1M after Vacc.,Serotype 11A (n=190,182,186,198) | 1.61 (1.39 to 1.85) | 2.63 (2.25 to 3.08) | 2.79 (2.35 to 3.33) | 3.13 (2.60 to 3.77) |
| Before Vacc.,Serotype 12F (n=188,183,186,198) | 0.01 (0.01 to 0.01) | 0.01 (0.01 to 0.01) | 0.01 (0.01 to 0.01) | 0.01 (0.01 to 0.01) |
| 1M after Vacc.,Serotype 12F (n=190,182,186,198) | 0.22 (0.18 to 0.27) | 0.38 (0.31 to 0.46) | 0.36 (0.29 to 0.44) | 0.28 (0.22 to 0.34) |
| Before Vacc.,Serotype 15B (n=188,182,186,198) | 0.02 (0.02 to 0.03) | 0.05 (0.04 to 0.07) | 0.20 (0.15 to 0.27) | 0.35 (0.27 to 0.45) |
| 1M after Vacc.,Serotype 15B (n=190,181,186,198) | 1.17 (0.97 to 1.40) | 3.96 (3.12 to 5.03) | 10.74 (8.49 to 13.60) | 18.79 (15.16 to 23.28) |
| Before Vacc.,Serotype 22F (n=188,183,186,198) | 0.01 (0.00 to 0.01) | 0.02 (0.01 to 0.02) | 0.08 (0.06 to 0.11) | 0.14 (0.11 to 0.19) |
| 1M after Vacc.,Serotype 22F (n=190,182,186,198) | 9.57 (8.12 to 11.29) | 12.46 (10.82 to 14.35) | 15.68 (13.45 to 18.29) | 12.36 (10.38 to 14.72) |
| Before Vacc.,Serotype 33F (n=188,183,185,196) | 0.02 (0.01 to 0.02) | 0.04 (0.03 to 0.05) | 0.10 (0.08 to 0.12) | 0.17 (0.14 to 0.22) |
| 1M after Vacc.,Serotype 33F (n=190,182,184,197) | 1.85 (1.55 to 2.19) | 3.03 (2.53 to 3.62) | 3.70 (3.10 to 4.41) | 3.75 (3.10 to 4.53) |

## Statistical analyses

No statistical analyses for this end point

## Secondary: GMFRs of Pneumococcal Serotype-Specific IgG Concentrations for the 13vPnC Serotypes From Before to 1 Month After Vaccination: Cohort 1 and 2

| | |
|---|---|
| End point title | GMFRs of Pneumococcal Serotype-Specific IgG Concentrations for the 13vPnC Serotypes From Before to 1 Month After Vaccination: Cohort 1 and 2[14] |

End point description:

Pneumococcal serotype-specific IgG concentrations were measured from serum samples for 13vPnC serotypes: 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F and 23F. GMFR was calculated as geometric mean of fold rise from before vaccination on Day 1 to 1 month after vaccination with 20vPnC. GMFRs and the corresponding 2-sided CIs were calculated by exponentiating the mean logarithm of the titres or fold rises and the corresponding CIs (based on the Student t distribution). EIP included all subjects who were eligible; received 20vPnC; at least 1 valid immunogenicity result from 1 month after vaccination collected within 27 to 56 days after vaccination for Cohorts 1-2; no other major protocol deviations. Here, "Number of Subjects Analysed" signifies subjects included in the EIP and n=subjects with valid assay results at both timepoints for the specified serotype.

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

End point timeframe:

Before vaccination to 1 month after vaccination

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analysed only for the specified reporting arms.

| **End point values** | Cohort 1: 20vPnC: >=15 to <24 Months | Cohort 2: 20vPnC: >=2 to <5 Years | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 190 | 183 | | |
| Units: Fold-rise | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Serotype 1 (n=189, 183) | 3.4 (3.0 to 3.9) | 20.6 (17.2 to 24.7) | | |

| | | | | |
|---|---|---|---|---|
| Serotype 3 (n=189, 183) | 3.9 (3.4 to 4.5) | 14.9 (12.4 to 17.9) | | |
| Serotype 4 (n=189, 183) | 4.3 (3.7 to 5.0) | 27.6 (22.7 to 33.5) | | |
| Serotype 5 (n=189, 183) | 3.6 (3.1 to 4.2) | 28.2 (23.0 to 34.6) | | |
| Serotype 6A (n=188, 183) | 4.8 (4.1 to 5.6) | 44.9 (35.8 to 56.3) | | |
| Serotype 6B (n=188, 183) | 5.0 (4.3 to 5.9) | 34.5 (28.3 to 42.0) | | |
| Serotype 7F (n=189, 183) | 3.0 (2.7 to 3.4) | 12.5 (10.5 to 14.9) | | |
| Serotype 9V (n=189, 183) | 3.8 (3.3 to 4.4) | 23.0 (19.0 to 27.8) | | |
| Serotype 14 (n=187, 183) | 2.9 (2.5 to 3.3) | 22.2 (18.0 to 27.4) | | |
| Serotype 18C (n=189, 183) | 4.2 (3.6 to 4.9) | 27.2 (22.5 to 32.9) | | |
| Serotype 19A (n=188, 183) | 6.9 (5.7 to 8.4) | 24.1 (19.0 to 30.6) | | |
| Serotype 19F (n=189, 183) | 5.2 (4.4 to 6.3) | 22.3 (17.2 to 28.8) | | |
| Serotype 23F (n=189, 183) | 5.6 (4.8 to 6.6) | 17.9 (14.6 to 21.9) | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: GMFRs of Pneumococcal Serotype-Specific IgG Concentrations for the 20vPnC Serotypes From Before to 1 Month After Vaccination: Cohort 3 and 4

| End point title | GMFRs of Pneumococcal Serotype-Specific IgG Concentrations for the 20vPnC Serotypes From Before to 1 Month After Vaccination: Cohort 3 and 4[15] |
|---|---|

End point description:

Pneumococcal serotype-specific IgG concentrations were measured from serum samples for 13vPnC serotypes: 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F and 23F; and 7 additional 20vPnC serotypes: 8, 10A, 11A, 12F, 15B, 22F and 33F. GMFR was calculated as geometric mean of fold rise from before vaccination on Day 1 to 1 month after vaccination with 20vPnC. GMFRs and the corresponding 2-sided CIs were calculated by exponentiating the mean logarithm of the titres or fold rises and the corresponding CIs (based on the Student t distribution). EIP included all subjects who were eligible; received 20vPnC; at least 1 valid immunogenicity result from 1 month after vaccination collected within 27 to 49 days after vaccination for Cohorts 3-4; no other major protocol deviations. Here, "Number of Subjects Analysed" signifies subjects included in the EIP and n= subjects with valid assay results at both timepoints for the specified serotype.

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

End point timeframe:

Before vaccination to 1 month after vaccination

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analysed only for the specified reporting arms.

| End point values | Cohort 3: 20vPnC: >=5 to <10 Years | Cohort 4: 20vPnC: >=10 to <18 Years | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 186 | 198 | | |
| Units: Fold-rise | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Serotype: 1 (n=186, 198) | 49.4 (41.6 to 58.6) | 44.2 (37.0 to 52.9) | | |
| Serotype: 3 (n=186, 198) | 5.9 (4.6 to 7.5) | 4.3 (3.5 to 5.2) | | |
| Serotype: 4 (n=186, 198) | 74.1 (61.4 to 89.4) | 52.0 (42.3 to 64.0) | | |
| Serotype: 5 (n=186, 198) | 107.0 (89.4 to 128.2) | 59.3 (47.6 to 73.9) | | |
| Serotype: 6A (n=184, 195) | 91.9 (67.7 to 124.9) | 72.5 (54.9 to 95.7) | | |
| Serotype: 6B (n=182, 195) | 127.9 (101.0 to 162.0) | 99.5 (77.1 to 128.3) | | |
| Serotype: 7F (n=186, 198) | 42.9 (36.1 to 51.1) | 30.0 (24.0 to 37.6) | | |
| Serotype: 9V (n=186, 198) | 80.3 (64.3 to 100.3) | 54.2 (42.7 to 68.9) | | |
| Serotype: 14 (n=186, 198) | 68.4 (53.4 to 87.7) | 96.7 (76.6 to 122.1) | | |
| Serotype: 18C (n=186, 198) | 93.7 (76.9 to 114.1) | 64.5 (52.3 to 79.4) | | |
| Serotype: 19A (n=186, 197) | 17.6 (13.2 to 23.4) | 16.2 (13.1 to 20.0) | | |
| Serotype: 19F (n=186, 198) | 15.2 (10.5 to 22.0) | 8.0 (6.0 to 10.7) | | |
| Serotype: 23F (n=186, 198) | 27.6 (21.0 to 36.3) | 31.4 (23.8 to 41.5) | | |
| Serotype: 8 (n=185, 196) | 55.2 (44.8 to 67.9) | 27.3 (21.9 to 33.9) | | |
| Serotype: 10A (n=186, 198) | 54.8 (44.4 to 67.7) | 35.9 (29.3 to 43.9) | | |
| Serotype: 11A (n=186, 198) | 23.6 (18.6 to 29.9) | 10.5 (8.5 to 12.9) | | |
| Serotype: 12F (n=186, 198) | 31.9 (26.7 to 38.3) | 21.4 (17.6 to 26.0) | | |
| Serotype: 15B (n=186, 198) | 52.6 (41.3 to 66.9) | 53.8 (43.1 to 67.1) | | |
| Serotype: 22F (n=186, 198) | 187.7 (134.6 to 261.7) | 86.2 (64.9 to 114.4) | | |
| Serotype: 33F (n=184, 195) | 39.3 (31.6 to 49.0) | 22.4 (18.2 to 27.6) | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Subjects With >=4-fold Rise in Pneumococcal Serotype-Specific OPA Titres for the 7 Additional Serotypes From Before to 1 Month After Vaccination: Cohorts 2, 3, and 4 Only

| End point title | Percentage of Subjects With >=4-fold Rise in Pneumococcal Serotype-Specific OPA Titres for the 7 Additional Serotypes |
|---|---|

| | |
|---|---|
| | From Before to 1 Month After Vaccination: Cohorts 2, 3, and 4 Only[16] |

End point description:

Pneumococcal serotype-specific OPA titres were measured from serum samples for 7 additional 20vPnC serotypes: 8, 10A, 11A, 12F, 15B, 22F and 33F. Percentage of subjects with >=4 fold rise in serotype-specific OPA titres from before vaccination to 1 month after vaccination with 20vPnC and the associated 2-sided 95% CI based on the Clopper and Pearson method was presented. EIP included all subjects who were eligible; received 20vPnC; at least 1 valid immunogenicity result from 1 month after vaccination collected within 27 to 56 days or 27 to 49 days after vaccination for Cohort 2 or Cohorts 3-4, respectively; no other major protocol deviations. Here, "Number of Subjects Analysed" signifies subjects included in the EIP and n=subjects with valid assay results at both timepoints for the specified serotype.

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

End point timeframe:

Before vaccination to 1 month after vaccination

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analysed only for the specified reporting arms.

| **End point values** | Cohort 2: 20vPnC: >=2 to <5 Years | Cohort 3: 20vPnC: >=5 to <10 Years | Cohort 4: 20vPnC: >=10 to <18 Years | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 183 | 186 | 198 | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Serotype: 8 (n=74, 153, 174) | 93.2 (84.9 to 97.8) | 92.2 (86.7 to 95.9) | 89.1 (83.5 to 93.3) | |
| Serotype: 10A (n=73, 134, 142) | 84.9 (74.6 to 92.2) | 80.6 (72.9 to 86.9) | 81.7 (74.3 to 87.7) | |
| Serotype: 11A (n=52, 136, 155) | 86.5 (74.2 to 94.4) | 66.2 (57.6 to 74.1) | 62.6 (54.5 to 70.2) | |
| Serotype: 12F (n=74, 154, 164) | 94.6 (86.7 to 98.5) | 96.8 (92.6 to 98.9) | 94.5 (89.8 to 97.5) | |
| Serotype: 15B (n=76, 142, 164) | 88.2 (78.7 to 94.4) | 89.4 (83.2 to 94.0) | 93.9 (89.1 to 97.0) | |
| Serotype: 22F (n=68, 137, 168) | 86.8 (76.4 to 93.8) | 87.6 (80.9 to 92.6) | 81.0 (74.2 to 86.6) | |
| Serotype: 33F (n=73, 144, 158) | 71.2 (59.4 to 81.2) | 79.9 (72.4 to 86.1) | 75.3 (67.8 to 81.8) | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Geometric Mean Titers (GMTs) of Pneumococcal Serotype-Specific OPA Titers for the 20vPnC Serotypes Before and 1 Month After Vaccination

| | |
|---|---|
| End point title | Geometric Mean Titers (GMTs) of Pneumococcal Serotype-Specific OPA Titers for the 20vPnC Serotypes Before and 1 Month After Vaccination |

End point description:

Pneumococcal serotype-specific OPA titres were measured from serum samples for 13vPnC serotypes: 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F; and 7 additional 20vPnC serotypes: 8, 10A, 11A, 12F, 15B, 22F and 33F. GMTs and 2-sided CIs were calculated by exponentiating the mean logarithm of the titres and the corresponding CIs (based on the Student t distribution). EIP included all subjects who were eligible; received 20vPnC; at least 1 valid immunogenicity result from 1 month after vaccination

collected within 27 to 56 days or 27 to 49 days after vaccination for Cohorts 1-2 or Cohorts 3-4,respectively; no other major protocol deviations. Here, "Number of Subjects Analysed" signifies subjects included in the EIP and n=subjects with valid OPA titres at the specified timepoint.

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

End point timeframe:

Before vaccination (Vacc.) and 1 month after vaccination (1M after Vacc.)

| **End point values** | Cohort 1: 20vPnC: >=15 to <24 Months | Cohort 2: 20vPnC: >=2 to <5 Years | Cohort 3: 20vPnC: >=5 to <10 Years | Cohort 4: 20vPnC: >=10 to <18 Years |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 190 | 183 | 186 | 198 |
| Units: Titer | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Before Vacc., Serotype 1 (n=46, 47, 93, 96) | 14 (11 to 18) | 12 (10 to 14) | 10 (9 to 11) | 11 (9 to 12) |
| 1M after Vacc.Serotype 1 (n=44,46, 93, 96) | 57 (39 to 84) | 360 (272 to 476) | 548 (455 to 660) | 396 (302 to 519) |
| Before Vacc., Serotype 3 (n=46, 47, 94, 95) | 21 (15 to 29) | 15 (11 to 22) | 29 (22 to 40) | 19 (14 to 24) |
| 1M after Vacc.Serotype 3 (n=44, 46, 92, 94) | 80 (62 to 103) | 150 (116 to 195) | 155 (135 to 178) | 105 (88 to 124) |
| Before Vacc., Serotype: 4 (n=41, 45, 82, 86) | 42 (24 to 75) | 34 (19 to 62) | 43 (27 to 67) | 34 (22 to 51) |
| 1M after Vacc.Serotype 4 (n=43, 44, 88, 93) | 563 (342 to 927) | 1729 (1188 to 2516) | 2328 (1942 to 2789) | 2290 (1822 to 2878) |
| Before Vacc., Serotype: 5 (n=46,47, 94, 96) | 18 (16 to 21) | 17 (15 to 20) | 15 (15 to 15) | 15 (15 to 16) |
| 1M after Vacc.Serotype 5, (n=44, 46, 92, 96) | 51 (38 to 68) | 198 (143 to 276) | 385 (324 to 458) | 216 (159 to 294) |
| Before Vacc., Serotype: 6A (n=46, 47, 90, 91) | 137 (77 to 243) | 96 (55 to 168) | 74 (51 to 106) | 64 (44 to 91) |
| 1M after Vacc.Serotype 6A (n=43, 46, 92, 96) | 1707 (1144 to 2547) | 5283 (3954 to 7060) | 8268 (6617 to 10331) | 9434 (7616 to 11686) |
| Before Vacc., Serotype: 6B (n=44, 43, 78, 90) | 110 (67 to 182) | 126 (72 to 219) | 156 (99 to 244) | 237 (155 to 363) |
| 1M after Vacc.Serotype 6B (n=44, 46, 90, 93) | 943 (611 to 1455) | 3273 (2390 to 4482) | 6569 (5367 to 8040) | 10085 (8263 to 12309) |
| Before Vacc., Serotype 7F (n=41, 45, 81, 86) | 705 (492 to 1010) | 996 (748 to 1327) | 541 (410 to 713) | 516 (381 to 698) |
| 1M after Vacc.Serotype 7F (n=42, 44, 87, 93) | 2635 (2105 to 3297) | 3409 (2552 to 4556) | 3981 (3446 to 4598) | 3326 (2878 to 3843) |
| Before Vacc., Serotype: 9V (n=39, 45, 84, 92) | 649 (350 to 1204) | 323 (202 to 515) | 410 (289 to 580) | 469 (330 to 667) |
| 1M after Vacc.Serotype 9V (n=43, 44, 87, 93) | 7686 (5718 to 10332) | 7210 (4781 to 10876) | 11717 (9262 to 14823) | 9627 (7492 to 12369) |
| Before Vacc., Serotype: 14 (n=46, 44, 90, 92) | 242 (151 to 387) | 300 (186 to 484) | 246 (172 to 353) | 97 (65 to 145) |
| 1M after Vacc.Serotype 14 (n=44, 46, 93, 96) | 1018 (748 to 1385) | 2506 (1932 to 3249) | 4610 (3688 to 5762) | 3925 (3153 to 4885) |
| Before Vacc., Serotype: 18C (n=38, 44, 76, 87) | 300 (147 to 613) | 139 (69 to 277) | 152 (89 to 261) | 73 (45 to 119) |
| 1M after Vacc.Serotype 18C (n=43, 44, 87, 93) | 3749 (2740 to 5131) | 5344 (3809 to 7498) | 6766 (5585 to 8197) | 3617 (2816 to 4645) |
| Before Vacc., Serotype: 19A (n=40, 47, 86, 90) | 138 (71 to 271) | 84 (45 to 156) | 117 (76 to 181) | 66 (44 to 100) |

| | | | | |
|---|---|---|---|---|
| 1M after Vacc.Serotype: 19A (n=43, 44, 88, 93) | 1708 (1192 to 2448) | 2640 (1943 to 3587) | 2162 (1786 to 2618) | 2212 (1801 to 2717) |
| Before Vacc., Serotype: 19F (n=45, 47, 94, 93) | 44 (31 to 61) | 44 (31 to 61) | 91 (66 to 125) | 57 (44 to 73) |
| 1M after Vacc.Serotype 19F (n=44, 46, 92, 96) | 267 (169 to 421) | 928 (618 to 1394) | 1095 (810 to 1479) | 551 (401 to 757) |
| Before Vacc., Serotype 23F (n=41, 46, 87, 92) | 139 (67 to 288) | 206 (108 to 394) | 87 (53 to 145) | 46 (29 to 73) |
| 1M after Vacc.Serotype 23F (n=43, 44, 88, 93) | 1936 (1385 to 2707) | 2493 (1757 to 3539) | 2213 (1751 to 2797) | 1842 (1391 to 2439) |
| Before Vacc., Serotype: 8 (n=86, 82, 164, 185) | 30 (24 to 39) | 39 (29 to 54) | 34 (28 to 42) | 35 (28 to 43) |
| 1M after Vacc.Serotyp 8 (n=85, 80, 175, 187) | 4758 (3763 to 6016) | 4428 (3467 to 5654) | 3870 (3302 to 4535) | 3125 (2680 to 3642) |
| Before Vacc., Serotype: 10A (n=84, 82, 158, 168) | 92 (60 to 141) | 275 (160 to 472) | 745 (519 to 1071) | 554 (395 to 777) |
| 1M after Vacc.Serotype 10A (n=86, 78, 159, 171) | 10626 (7825 to 14429) | 14345 (10473 to 19649) | 21102 (17238 to 25833) | 17417 (14301 to 21214) |
| Before Vacc., Serotype 11A (n=68, 60, 147, 165) | 88 (60 to 127) | 436 (237 to 800) | 1347 (962 to 1887) | 765 (543 to 1076) |
| 1M after Vacc.Serotype: 11A (n=84, 78, 172, 186) | 13350 (10540 to 16910) | 14093 (9904 to 20054) | 16882 (13650 to 20880) | 11677 (9751 to 13982) |
| Serotype: 12F (n=92, 86, 174, 182) | 38 (29 to 50) | 37 (27 to 50) | 48 (38 to 60) | 46 (36 to 59) |
| 1M after Vacc.Serotype: 12F (n=84, 76, 164, 180) | 16924 (13400 to 21376) | 13257 (9463 to 18572) | 23860 (19002 to 29959) | 20250 (16861 to 24320) |
| Before Vacc., Serotype: 15B (n=94, 84, 163, 187) | 30 (21 to 45) | 111 (63 to 197) | 79 (54 to 115) | 45 (33 to 61) |
| 1M after Vacc.Serotype: 15B (n=86, 80, 163, 174) | 22951 (17380 to 30307) | 27095 (19557 to 37538) | 25729 (19647 to 33695) | 21496 (16697 to 27672) |
| Before Vacc., Serotype: 22F (n=87, 80, 161, 184) | 21 (13 to 33) | 104 (55 to 194) | 259 (170 to 394) | 243 (161 to 366) |
| 1M after Vacc.Serotype 22F (n=81, 74, 158, 179) | 22464 (16840 to 29967) | 25573 (18096 to 36141) | 33615 (26198 to 43130) | 27922 (22622 to 34463) |
| Before Vacc., Serotype: 33F (n=91, 85, 170, 177) | 1154 (861 to 1548) | 2179 (1694 to 2804) | 3334 (2847 to 3905) | 2895 (2448 to 3424) |
| 1M after Vacc.Serotype 33F (n=81, 76, 155, 171) | 23431 (17375 to 31598) | 28076 (19255 to 40938) | 45921 (36768 to 57353) | 32363 (26219 to 39946) |

### Statistical analyses

No statistical analyses for this end point

## Secondary: GMFRs of Pneumococcal Serotype-Specific OPA Titres for the 20vPnC Serotypes From Before to 1 Month After Vaccination: Cohorts 1 and 2

| End point title | GMFRs of Pneumococcal Serotype-Specific OPA Titres for the 20vPnC Serotypes From Before to 1 Month After Vaccination: Cohorts 1 and 2[17] |
|---|---|

End point description:

Pneumococcal serotype-specific OPA titres were measured from serum samples for 13vPnC serotypes: 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F; and 7 additional 20vPnC serotypes: 8, 10A, 11A, 12F, 15B, 22F and 33F. GMFR was calculated as geometric mean of fold rise from before vaccination on Day 1 to 1 month after vaccination with 20vPnC. GMFRs and the corresponding 2-sided CIs were calculated by exponentiating the mean logarithm of the titres or fold rises and the corresponding CIs (based on the Student t distribution). EIP included all subjects who were eligible; received 20vPnC; at least 1 valid immunogenicity result from 1 month after vaccination collected within 27 to 56 days after vaccination for Cohorts 1-2; no other major protocol deviations. Here, 'Number of Subjects Analysed' signifies subjects included in the EIP and n=subjects with valid assay results at both timepoints for the specified serotype.

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

End point timeframe:

Before vaccination to 1 month after vaccination

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This endpoint was planned to be analysed only for the specified reporting arms.

| **End point values** | Cohort 1: 20vPnC: >=15 to <24 Months | Cohort 2: 20vPnC: >=2 to <5 Years | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 190 | 183 | | |
| Units: Fold rise | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Serotype 1 (n=42, 46) | 4.1 (2.9 to 6.0) | 29.8 (21.2 to 41.9) | | |
| Serotype 3 (n=42, 46) | 3.7 (2.6 to 5.3) | 9.6 (7.1 to 13.1) | | |
| Serotype 4 (n=40, 41) | 13.2 (7.0 to 25.0) | 50.0 (26.7 to 93.6) | | |
| Serotype 5 (n=42, 46) | 2.8 (2.0 to 3.8) | 11.4 (8.2 to 16.0) | | |
| Serotype 6A (n=41, 46) | 12.7 (8.1 to 20.0) | 52.9 (30.8 to 90.9) | | |
| Serotype 6B (n=40, 42) | 7.8 (4.6 to 13.2) | 24.4 (14.4 to 41.2) | | |
| Serotype 7F (n=39, 41) | 3.6 (2.5 to 5.2) | 3.6 (2.7 to 4.8) | | |
| Serotype 9V (n=38, 42) | 11.5 (6.2 to 21.3) | 23.1 (14.7 to 36.5) | | |
| Serotype 14 (n=42, 43) | 3.9 (2.5 to 6.1) | 8.3 (5.1 to 13.4) | | |
| Serotype 18C (n=38, 40) | 12.7 (6.6 to 24.5) | 40.6 (20.7 to 79.6) | | |
| Serotype 19A (n=39, 43) | 11.1 (6.2 to 19.8) | 33.5 (17.3 to 65.0) | | |
| Serotype 19F (n=41, 46) | 5.7 (3.3 to 9.7) | 21.0 (13.0 to 33.9) | | |
| Serotype 23F (n=40, 42) | 12.5 (6.7 to 23.6) | 10.7 (6.2 to 18.5) | | |
| Serotype 8 (n=76, 74) | 155.9 (110.4 to 220.2) | 105.4 (67.6 to 164.3) | | |
| Serotype 10A (n=76, 73) | 121.7 (74.7 to 198.4) | 53.3 (28.7 to 99.0) | | |
| Serotype 11A (n=60, 52) | 161.4 (115.7 to 225.2) | 34.7 (17.1 to 70.4) | | |
| Serotype 12F (n=81, 74) | 437.2 (307.0 to 622.7) | 319.9 (193.9 to 527.9) | | |
| Serotype 15B (n=84, 76) | 717.6 (449.8 to 1144.6) | 294.4 (149.1 to 581.3) | | |
| Serotype 22F (n=74, 68) | 983.6 (580.9 to 1665.5) | 224.6 (104.9 to 480.9) | | |
| Serotype 33F (n=78, 73) | 18.8 (13.1 to 27.2) | 12.4 (7.4 to 20.7) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: GMFRs of Pneumococcal Serotype-Specific OPA Titres for the 13vPnC Serotypes From Before to 1 Month After Vaccination: Cohorts 3 and 4

| End point title | GMFRs of Pneumococcal Serotype-Specific OPA Titres for the 13vPnC Serotypes From Before to 1 Month After Vaccination: Cohorts 3 and 4[18] |
|---|---|

End point description:

Pneumococcal serotype-specific OPA titres were measured for 13vPnC serotypes: 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F. GMFR was calculated as geometric mean of fold rise from before vaccination on Day 1 to 1 month after vaccination with 20vPnC. GMFRs and the corresponding 2-sided CIs were calculated by exponentiating the mean logarithm of the titres or fold rises and the corresponding CIs (based on the Student t distribution). EIP included all subjects who were eligible; received 20vPnC; at least 1 valid immunogenicity result from 1 month after vaccination collected within 27 to 49 days after vaccination for Cohorts 3-4; no other major protocol deviations. Here, "Number of Subjects Analysed" signifies subjects included in the EIP and n=subjects with valid assay results at both timepoints for the specified serotype.

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

End point timeframe:

Before vaccination to 1 month after vaccination

Notes:

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analysed only for the specified reporting arms.

| **End point values** | Cohort 3: 20vPnC: >=5 to <10 Years | Cohort 4: 20vPnC: >=10 to <18 Years | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 186 | 198 | | |
| Units: Fold rise | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Serotype 1 (n=91, 96) | 55.2 (45.1 to 67.4) | 37.3 (28.7 to 48.6) | | |
| Serotype 3 (n=91, 93) | 5.3 (3.9 to 7.2) | 5.8 (4.5 to 7.5) | | |
| Serotype 4 (n=80, 86) | 50.2 (31.6 to 79.5) | 65.6 (41.4 to 103.7) | | |
| Serotype 5 (n=91, 96) | 26.7 (22.4 to 31.8) | 14.4 (10.5 to 19.6) | | |
| Serotype 6A (n=87, 91) | 110.3 (68.7 to 177.1) | 147.9 (96.0 to 228.0) | | |
| Serotype 6B (n=73, 87) | 38.8 (22.7 to 66.3) | 42.0 (26.1 to 67.6) | | |
| Serotype 7F (n=78, 86) | 7.0 (5.3 to 9.3) | 6.2 (4.4 to 8.8) | | |
| Serotype 9V (n=82, 92) | 28.9 (19.7 to 42.5) | 20.4 (13.4 to 31.0) | | |
| Serotype 14 (n=88, 92) | 18.1 (12.2 to 26.8) | 38.9 (25.1 to 60.3) | | |
| Serotype 18C (n=74, 87) | 46.2 (26.8 to 79.6) | 47.3 (28.7 to 78.0) | | |
| Serotype 19A (n=84, 90) | 17.5 (10.8 to 28.3) | 33.1 (20.7 to 53.1) | | |
| Serotype 19F (n=91, 93) | 11.7 (7.4 to 18.5) | 10.0 (6.7 to 15.0) | | |
| Serotype 23F (n=85, 92) | 26.9 (16.3 to 44.5) | 39.4 (23.7 to 65.7) | | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Local reactions and systemic events (systematic assessment): within 7 days after vaccination; SAEs (non-systematic assessment): from Day1 up to 6 months after vaccination and other AEs (non-systematic assessment): from Day1 up to 1 month after vaccination

Adverse event reporting additional description:

The same event may appear as both an AE and a SAE. However, what is presented are distinct events. An event may be categorized as serious in one subject and as non-serious in another subject, or one subject may have experienced both a serious and non-serious event during the study.

| | |
|---|---|
| Assessment type | Non-systematic |

### Dictionary used

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

### Reporting groups

| | |
|---|---|
| Reporting group title | Cohort 1: 20vPnC: >=15 to <24 Months |

Reporting group description:

Subjects aged >=15 months to <24 months who have been previously vaccinated with at least 3 doses of 13vPnC, were administered a single dose of 0.5 mL 20vPnC intramuscularly on Day 1.

| | |
|---|---|
| Reporting group title | Cohort 2: 20vPnC: >=2 to <5 Years |

Reporting group description:

Subjects aged >=2 to <5 years who have been previously vaccinated with at least 3 doses of 13vPnC, were administered a single dose of 0.5 mL 20vPnC intramuscularly on Day 1.

| | |
|---|---|
| Reporting group title | Cohort 3: 20vPnC: >=5 to <10 Years |

Reporting group description:

Subjects aged >=5 to <10 years regardless of previous vaccination status with 7vPnC or 13vPnC, were administered a single dose of 0.5 mL 20vPnC intramuscularly into the left arm on Day 1.

| | |
|---|---|
| Reporting group title | Cohort 4: 20vPnC: >=10 to <18 Years |

Reporting group description:

Subjects aged >=10 to <18 years regardless of previous vaccination status with 7vPnC or 13vPnC, were administered a single dose of 0.5 mL 20vPnC intramuscularly into the left arm on Day 1.

| Serious adverse events | Cohort 1: 20vPnC: >=15 to <24 Months | Cohort 2: 20vPnC: >=2 to <5 Years | Cohort 3: 20vPnC: >=5 to <10 Years |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 2 / 209 (0.96%) | 0 / 216 (0.00%) | 0 / 201 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Papillary thyroid cancer | | | |
| subjects affected / exposed | 0 / 209 (0.00%) | 0 / 216 (0.00%) | 0 / 201 (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 |
| Injury, poisoning and procedural complications | | | |

| | | | |
|---|---|---|---|
| Near drowning | | | |
| subjects affected / exposed | 1 / 209 (0.48%) | 0 / 216 (0.00%) | 0 / 201 (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 |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 0 / 209 (0.00%) | 0 / 216 (0.00%) | 0 / 201 (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 |
| Febrile convulsion | | | |
| subjects affected / exposed | 1 / 209 (0.48%) | 0 / 216 (0.00%) | 0 / 201 (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 | | | |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 209 (0.00%) | 0 / 216 (0.00%) | 0 / 201 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| **Serious adverse events** | Cohort 4: 20vPnC: >=10 to <18 Years | | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 3 / 205 (1.46%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Papillary thyroid cancer | | | |
| subjects affected / exposed | 1 / 205 (0.49%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Injury, poisoning and procedural complications | | | |
| Near drowning | | | |
| subjects affected / exposed | 0 / 205 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |

| | | | |
|---|---|---|---|
| Headache | | | |
| subjects affected / exposed | 1 / 205 (0.49%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Febrile convulsion | | | |
| subjects affected / exposed | 0 / 205 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Appendicitis | | | |
| subjects affected / exposed | 1 / 205 (0.49%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| **Non-serious adverse events** | Cohort 1: 20vPnC: >=15 to <24 Months | Cohort 2: 20vPnC: >=2 to <5 Years | Cohort 3: 20vPnC: >=5 to <10 Years |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 173 / 209 (82.78%) | 163 / 216 (75.46%) | 178 / 201 (88.56%) |
| Nervous system disorders | | | |
| Headache (HEADACHE) | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 209 (0.00%) | 12 / 216 (5.56%) | 37 / 201 (18.41%) |
| occurrences (all) | 0 | 13 | 45 |
| Hypersomnia (INCREASED SLEEP) | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 85 / 209 (40.67%) | 0 / 216 (0.00%) | 0 / 201 (0.00%) |
| occurrences (all) | 104 | 0 | 0 |
| General disorders and administration site conditions | | | |
| Injection site erythema (REDNESS) | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 77 / 209 (36.84%) | 84 / 216 (38.89%) | 74 / 201 (36.82%) |
| occurrences (all) | 84 | 86 | 79 |
| Injection site pain (PAIN) | | | |

| | | | |
|---|---|---|---|
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 107 / 209 (51.20%) | 142 / 216 (65.74%) | 165 / 201 (82.09%) |
| occurrences (all) | 115 | 157 | 178 |
| Injection site swelling (SWELLING) | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 45 / 209 (21.53%) | 50 / 216 (23.15%) | 54 / 201 (26.87%) |
| occurrences (all) | 51 | 54 | 57 |
| Pyrexia (FEVER) | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 24 / 209 (11.48%) | 7 / 216 (3.24%) | 1 / 201 (0.50%) |
| occurrences (all) | 25 | 9 | 1 |
| Fatigue (FATIGUE) | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 209 (0.00%) | 80 / 216 (37.04%) | 56 / 201 (27.86%) |
| occurrences (all) | 0 | 98 | 76 |
| Psychiatric disorders | | | |
| Irritability (IRRITABILITY) | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 126 / 209 (60.29%) | 0 / 216 (0.00%) | 0 / 201 (0.00%) |
| occurrences (all) | 170 | 0 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia (JOINT PAIN) | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 209 (0.00%) | 8 / 216 (3.70%) | 13 / 201 (6.47%) |
| occurrences (all) | 0 | 9 | 14 |
| Myalgia (MUSCLE PAIN) | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 209 (0.00%) | 57 / 216 (26.39%) | 78 / 201 (38.81%) |
| occurrences (all) | 0 | 63 | 86 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite (DECREASED APPETITE) | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 51 / 209 (24.40%) | 0 / 216 (0.00%) | 0 / 201 (0.00%) |
| occurrences (all) | 72 | 0 | 0 |

| **Non-serious adverse events** | Cohort 4: 20vPnC: >=10 to <18 Years | | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 186 / 205 (90.73%) | | |
| Nervous system disorders | | | |
| Headache (HEADACHE) | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 60 / 205 (29.27%) | | |
| occurrences (all) | 75 | | |
| Hypersomnia (INCREASED SLEEP) | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 205 (0.00%) | | |
| occurrences (all) | 0 | | |
| General disorders and administration site conditions | | | |
| Injection site erythema (REDNESS) | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 31 / 205 (15.12%) | | |
| occurrences (all) | 32 | | |
| Injection site pain (PAIN) | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 168 / 205 (81.95%) | | |
| occurrences (all) | 175 | | |
| Injection site swelling (SWELLING) | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 32 / 205 (15.61%) | | |
| occurrences (all) | 34 | | |
| Pyrexia (FEVER) | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 205 (0.00%) | | |
| occurrences (all) | 0 | | |
| Fatigue (FATIGUE) | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 57 / 205 (27.80%) | | |
| occurrences (all) | 66 | | |
| Psychiatric disorders | | | |

| | | | |
|---|---|---|---|
| Irritability (IRRITABILITY)<br>alternative assessment type: Systematic<br>subjects affected / exposed<br>occurrences (all) | <br><br>0 / 205 (0.00%)<br>0 | | |
| Musculoskeletal and connective tissue disorders<br>Arthralgia (JOINT PAIN)<br>alternative assessment type: Systematic<br>subjects affected / exposed<br>occurrences (all)<br><br>Myalgia (MUSCLE PAIN)<br>alternative assessment type: Systematic<br>subjects affected / exposed<br>occurrences (all) | <br><br><br>17 / 205 (8.29%)<br>17<br><br><br><br>99 / 205 (48.29%)<br>108 | | |
| Metabolism and nutrition disorders<br>Decreased appetite (DECREASED APPETITE)<br>alternative assessment type: Systematic<br>subjects affected / exposed<br>occurrences (all) | <br><br><br>0 / 205 (0.00%)<br>0 | | |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 18 October 2021 | -To be consistent with the European PIP modification approved in August 2021 added 2 secondary immunogenicity endpoints.<br>-Added 2 exploratory immunogenicity endpoints for additional description of the immune response.<br>- Clarified that the primary immunogenicity endpoints and the additional secondary endpoints are addressing consistencies with the approved European PIP modification. |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported