



Clinical trial results:

A Phase 3, Randomized, Double-Blind Trial to Evaluate the Safety and Immunogenicity of a 20-valent Pneumococcal Conjugate Vaccine in Healthy Infants

Summary

| | |
|--------------------------|-------------------|
| EudraCT number | 2019-003305-10 |
| Trial protocol | Outside EU/EEA |
| Global end of trial date | 02 September 2022 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 (current) |
| This version publication date | 15 March 2023 |
| First version publication date | 15 March 2023 |

Trial information

Trial identification

| | |
|-----------------------|----------|
| Sponsor protocol code | B7471011 |
|-----------------------|----------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT04382326 |
| 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 Inc., Pfizer ClinicalTrials.gov Call Center, 001 18007181021, ClinicalTrials.gov_Inquiries@pfizer.com |
| Scientific contact | Pfizer Inc., Pfizer ClinicalTrials.gov Call Center, 001 18007181021, ClinicalTrials.gov_Inquiries@pfizer.com |

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

| | |
|--|-------------------|
| Analysis stage | Final |
| Date of interim/final analysis | 07 October 2022 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 02 September 2022 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

Safety: To describe the safety profile of 20vPnC. Safety assessments included local reactions, systemic events and adverse events.

Immunogenicity: Noninferiority of IgG GMCs (2-fold criterion) at 1 month after Dose 4 (co-primary) and 1 month after Dose 3 (key secondary); Percentage of participants with predefined IgG concentrations 1 month after Dose 3 (co-primary; 10% Noninferiority criterion); Noninferiority of percentage of participants with prespecified antibody levels to specific concomitant vaccine antigens 1 month after Dose 3. The 7 additional serotypes in the 20vPnC group were compared with the lowest result among vaccine serotypes in the 13vPnC group for noninferiority evaluation of pneumococcal endpoints.

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 | 20 May 2020 |
| 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 | United States: 1774 |
| Country: Number of subjects enrolled | Puerto Rico: 214 |
| Worldwide total number of subjects | 1988 |
| 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) | 1988 |
| Children (2-11 years) | 0 |

| | |
|---------------------------|---|
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 1997 subjects were enrolled and randomized in the study. Six subjects did not receive any study vaccine. Three subjects who received incorrect study vaccine during the study were excluded.

Period 1

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

Arms

| | |
|------------------------------|--------|
| Are arms mutually exclusive? | Yes |
| Arm title | 20vPnC |

Arm description:

Infants 42 to 98 days of age were enrolled to receive 4 doses of 0.5 millilitre (mL) 20-valent Pneumococcal Conjugate Vaccine (20vPnC) intramuscularly. Dose 1 was given at enrollment and Dose 2 and 3 were given 42 to 63 days from the previous dose. Dose 4 was administered at 365 to 455 days of age.

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | 20-valent pneumococcal conjugate vaccine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Subjects received a single dose (0.5 mL) of 20vPnC intramuscularly into the anterolateral thigh muscle of the left leg at each vaccination visit (Doses 1, 2, 3, and 4 at Visits 1, 2, 3, and 5, respectively).

| | |
|------------------|--------|
| Arm title | 13vPnC |
|------------------|--------|

Arm description:

Infants 42 to 98 days of age were enrolled to receive 4 doses of 0.5 millilitre (mL) 13-valent Pneumococcal Conjugate Vaccine (13vPnC) intramuscularly. Dose 1 was given at enrollment and Dose 2 and 3 were given 42 to 63 days from the previous dose. Dose 4 was administered at 365 to 455 days of age.

| | |
|--|--|
| Arm type | Active comparator |
| Investigational medicinal product name | 13-valent pneumococcal conjugate vaccine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Subjects received a single dose (0.5 mL) of 13vPnC intramuscularly into the anterolateral thigh muscle of the left leg at each vaccination visit (Doses 1, 2, 3, and 4 at Visits 1, 2, 3, and 5, respectively).

| Number of subjects in period 1 | 20vPnC | 13vPnC |
|---------------------------------------|--------|--------|
| Started | 1001 | 987 |
| Completed | 821 | 799 |
| Not completed | 180 | 188 |
| Physician decision | - | 1 |
| Adverse Event, not serious | 1 | 2 |
| Withdrawal By Parent/Guardian | 50 | 54 |
| Adverse event, non-fatal | 1 | 1 |
| Unspecified | 1 | - |
| No Longer Meets Eligibility Criteria | 50 | 44 |
| Lost to follow-up | 48 | 63 |
| Protocol deviation | 29 | 23 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|--------|
| Reporting group title | 20vPnC |
|-----------------------|--------|

Reporting group description:

Infants 42 to 98 days of age were enrolled to receive 4 doses of 0.5 millilitre (mL) 20-valent Pneumococcal Conjugate Vaccine (20vPnC) intramuscularly. Dose 1 was given at enrollment and Dose 2 and 3 were given 42 to 63 days from the previous dose. Dose 4 was administered at 365 to 455 days of age.

| | |
|-----------------------|--------|
| Reporting group title | 13vPnC |
|-----------------------|--------|

Reporting group description:

Infants 42 to 98 days of age were enrolled to receive 4 doses of 0.5 millilitre (mL) 13-valent Pneumococcal Conjugate Vaccine (13vPnC) intramuscularly. Dose 1 was given at enrollment and Dose 2 and 3 were given 42 to 63 days from the previous dose. Dose 4 was administered at 365 to 455 days of age.

| Reporting group values | 20vPnC | 13vPnC | Total |
|--|----------|----------|-------|
| Number of subjects | 1001 | 987 | 1988 |
| Age Categorical Units: Participants | | | |
| Infants and Toddlers(28 days - 23 months) Days | 1001 | 987 | 1988 |
| Age Continuous Units: Days | | | |
| arithmetic mean | 65.9 | 65.6 | - |
| standard deviation | ± 7.98 | ± 7.12 | - |
| Sex: Female, Male Units: Participants | | | |
| Female | 483 | 482 | 965 |
| Male | 518 | 505 | 1023 |
| Race/Ethnicity, Customized Units: Subjects | | | |
| White | 754 | 742 | 1496 |
| Black or African American | 110 | 108 | 218 |
| Asian | 16 | 16 | 32 |
| American Indian or Alaska Native | 4 | 3 | 7 |
| Native Hawaiian or other Pacific Islander | 2 | 2 | 4 |
| Multiracial | 68 | 73 | 141 |
| Not reported | 47 | 43 | 90 |
| Ethnicity (NIH/OMB) Units: Subjects | | | |
| Hispanic/Latino | 312 | 293 | 605 |
| Non-Hispanic/non-Latino | 661 | 659 | 1320 |
| Not reported | 28 | 35 | 63 |
| Age Range Units: Days | | | |
| median | 64.0 | 64.0 | - |
| full range (min-max) | 42 to 97 | 43 to 96 | - |

End points

End points reporting groups

| | |
|--|--------|
| Reporting group title | 20vPnC |
| Reporting group description: | |
| <p>Infants 42 to 98 days of age were enrolled to receive 4 doses of 0.5 millilitre (mL) 20-valent Pneumococcal Conjugate Vaccine (20vPnC) intramuscularly. Dose 1 was given at enrollment and Dose 2 and 3 were given 42 to 63 days from the previous dose. Dose 4 was administered at 365 to 455 days of age.</p> | |
| Reporting group title | 13vPnC |
| Reporting group description: | |
| <p>Infants 42 to 98 days of age were enrolled to receive 4 doses of 0.5 millilitre (mL) 13-valent Pneumococcal Conjugate Vaccine (13vPnC) intramuscularly. Dose 1 was given at enrollment and Dose 2 and 3 were given 42 to 63 days from the previous dose. Dose 4 was administered at 365 to 455 days of age.</p> | |

Primary: Percentage of Subjects With Local Reactions Within 7 Days After Dose 1

| | |
|--|---|
| End point title | Percentage of Subjects With Local Reactions Within 7 Days After Dose 1 ^[1] |
| End point description: | |
| <p>Local reactions were recorded using an electronic diary. Local reactions included redness, swelling and pain at the injection site. Redness and swelling were graded as mild (0.5 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 example, whimpered, winced, protested, or withdrew), moderate (hurt if gently touched, with crying), and severe (caused limitation of limb movement). Safety population included all the subjects who received at least 1 dose of the investigational product (IP) with safety follow up after any dose. Here, 'Number of Subjects Analyzed' = number of subjects with any electronic diary (e-diary) data reported after Dose 1.</p> | |
| End point type | Primary |
| End point timeframe: | |
| Within 7 days after Dose 1 | |
| Notes: | |
| <p>[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.</p> <p>Justification: Only descriptive data was planned to be analyzed for this endpoint.</p> | |

| End point values | 20vPnC | 13vPnC | | |
|----------------------------------|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 993 | 974 | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Redness: Any | 25.5 (22.8 to 28.3) | 24.6 (22.0 to 27.5) | | |
| Redness: Mild | 21.5 (18.9 to 24.1) | 22.3 (19.7 to 25.0) | | |
| Redness: Moderate | 4.0 (2.9 to 5.4) | 2.4 (1.5 to 3.5) | | |
| Redness: Severe | 0 (0.0 to 0.4) | 0 (0.0 to 0.4) | | |
| Swelling: Any | 16.4 (14.2 to 18.9) | 18.8 (16.4 to 21.4) | | |
| Swelling: Mild | 11.5 (9.6 to 13.6) | 14.7 (12.5 to 17.1) | | |
| Swelling: Moderate | 4.8 (3.6 to 6.4) | 4.1 (2.9 to 5.6) | | |
| Swelling: Severe | 0.1 (0.0 to 0.6) | 0 (0.0 to 0.4) | | |

| | | | | |
|--------------------------------------|---------------------|---------------------|--|--|
| Pain at the injection site: Any | 49.1 (46.0 to 52.3) | 45.3 (42.1 to 48.5) | | |
| Pain at the injection site: Mild | 30.6 (27.8 to 33.6) | 30.4 (27.5 to 33.4) | | |
| Pain at the injection site: Moderate | 18.4 (16.1 to 21.0) | 14.9 (12.7 to 17.3) | | |
| Pain at the injection site: Severe | 0.1 (0.0 to 0.6) | 0 (0.0 to 0.4) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Local Reactions Within 7 Days After Dose 2

| | |
|-----------------|---|
| End point title | Percentage of Subjects With Local Reactions Within 7 Days After Dose 2 ^[2] |
|-----------------|---|

End point description:

Local reactions were recorded using an electronic diary. Local reactions included redness, swelling and pain at the injection site. Redness and swelling were graded as mild (0.5 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 example, whimpered, winced, protested, or withdrew), moderate (hurt if gently touched, with crying), and severe (caused limitation of limb movement). Safety population included all the subjects who received at least 1 dose of the investigational product (IP) with safety follow up after any dose. Here, 'Number of Subjects Analyzed' = number of subjects with any electronic diary (e-diary) data reported after Dose 2.

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

End point timeframe:

Within 7 Days After Dose 2

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: Only descriptive data was planned to be analyzed for this endpoint.

| End point values | 20vPnC | 13vPnC | | |
|--------------------------------------|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 940 | 924 | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Redness: Any | 23.2 (20.5 to 26.0) | 26.4 (23.6 to 29.4) | | |
| Redness: Mild | 21.2 (18.6 to 23.9) | 23.1 (20.4 to 25.9) | | |
| Redness: Moderate | 2.0 (1.2 to 3.1) | 3.4 (2.3 to 4.7) | | |
| Redness: Severe | 0 (0.0 to 0.4) | 0 (0.0 to 0.4) | | |
| Swelling: Any | 15.5 (13.3 to 18.0) | 17.3 (14.9 to 19.9) | | |
| Swelling: Mild | 11.5 (9.5 to 13.7) | 13.5 (11.4 to 15.9) | | |
| Swelling: Moderate | 4.0 (2.9 to 5.5) | 3.8 (2.7 to 5.2) | | |
| Swelling: Severe | 0 (0.0 to 0.4) | 0 (0.0 to 0.4) | | |
| Pain at the injection site: Any | 44.0 (40.8 to 47.3) | 41.7 (38.5 to 44.9) | | |
| Pain at the injection site: Mild | 29.3 (26.4 to 32.3) | 27.7 (24.8 to 30.7) | | |
| Pain at the injection site: Moderate | 14.8 (12.6 to 17.2) | 14.0 (11.8 to 16.4) | | |

| | | | | |
|------------------------------------|----------------|----------------|--|--|
| Pain at the injection site: Severe | 0 (0.0 to 0.4) | 0 (0.0 to 0.4) | | |
|------------------------------------|----------------|----------------|--|--|

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Local Reactions Within 7 Days After Dose 3

| | |
|---|---|
| End point title | Percentage of Subjects With Local Reactions Within 7 Days After Dose 3 ^[3] |
| End point description: | |
| Local reactions were recorded using an electronic diary. Local reactions included redness, swelling and pain at the injection site. Redness and swelling were graded as mild (0.5 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 example, whimpered, winced, protested, or withdrew), moderate (hurt if gently touched, with crying), and severe (caused limitation of limb movement). Safety population included all the subjects who received at least 1 dose of the investigational product (IP) with safety follow up after any dose. Here, 'Number of Subjects Analyzed' = number of subjects with any electronic diary (e-diary) data reported after Dose 3. | |
| End point type | Primary |
| End point timeframe: | |
| Within 7 days after Dose 3 | |

Notes:

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

Justification: Only descriptive data was planned to be analyzed for this endpoint.

| End point values | 20vPnC | 13vPnC | | |
|--------------------------------------|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 914 | 901 | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Redness: Any | 25.4 (22.6 to 28.3) | 27.2 (24.3 to 30.2) | | |
| Redness: Mild | 21.1 (18.5 to 23.9) | 23.5 (20.8 to 26.4) | | |
| Redness: Moderate | 4.3 (3.1 to 5.8) | 3.7 (2.5 to 5.1) | | |
| Redness: Severe | 0 (0.0 to 0.4) | 0 (0.0 to 0.4) | | |
| Swelling: Any | 17.1 (14.7 to 19.7) | 17.6 (15.2 to 20.3) | | |
| Swelling: Mild | 12.5 (10.4 to 14.8) | 13.8 (11.6 to 16.2) | | |
| Swelling: Moderate | 4.6 (3.3 to 6.2) | 3.8 (2.6 to 5.2) | | |
| Swelling: Severe | 0 (0.0 to 0.4) | 0.1 (0.0 to 0.6) | | |
| Pain at the injection site: Any | 38.6 (35.5 to 41.9) | 39.0 (35.8 to 42.2) | | |
| Pain at the injection site: Mild | 25.7 (22.9 to 28.7) | 25.5 (22.7 to 28.5) | | |
| Pain at the injection site: Moderate | 12.9 (10.8 to 15.3) | 13.4 (11.3 to 15.8) | | |
| Pain at the injection site: Severe | 0 (0.0 to 0.4) | 0 (0.0 to 0.4) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Local Reactions Within 7 Days After Dose 4

| | |
|-----------------|---|
| End point title | Percentage of Subjects With Local Reactions Within 7 Days After Dose 4 ^[4] |
|-----------------|---|

End point description:

Local reactions were recorded using an electronic diary. Local reactions included redness, swelling and pain at the injection site. Redness and swelling were graded as mild (0.5 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 example, whimpered, winced, protested, or withdrew), moderate (hurt if gently touched, with crying), and severe (caused limitation of limb movement). Safety population included all the subjects who received at least 1 dose of the investigational product (IP) with safety follow up after any dose. Here, 'Number of Subjects Analyzed' = number of subjects with any electronic diary (e-diary) data reported after Dose 4.

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

End point timeframe:

Within 7 days after Dose 4

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: Only descriptive data was planned to be analyzed for this endpoint.

| End point values | 20vPnC | 13vPnC | | |
|--------------------------------------|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 826 | 815 | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Redness: Any | 23.5 (20.6 to 26.5) | 26.6 (23.6 to 29.8) | | |
| Redness: Mild | 19.6 (17.0 to 22.5) | 22.0 (19.2 to 25.0) | | |
| Redness: Moderate | 3.9 (2.7 to 5.4) | 4.7 (3.3 to 6.3) | | |
| Redness: Severe | 0 (0.0 to 0.4) | 0 (0.0 to 0.5) | | |
| Swelling: Any | 14.9 (12.5 to 17.5) | 17.3 (14.8 to 20.1) | | |
| Swelling: Mild | 10.7 (8.6 to 13.0) | 13.6 (11.3 to 16.2) | | |
| Swelling: Moderate | 4.2 (3.0 to 5.8) | 3.7 (2.5 to 5.2) | | |
| Swelling: Severe | 0 (0.0 to 0.4) | 0 (0.0 to 0.5) | | |
| Pain at the injection site: Any | 35.7 (32.4 to 39.1) | 35.8 (32.5 to 39.2) | | |
| Pain at the injection site: Mild | 24.1 (21.2 to 27.2) | 27.1 (24.1 to 30.3) | | |
| Pain at the injection site: Moderate | 11.3 (9.2 to 13.6) | 8.7 (6.9 to 10.9) | | |
| Pain at the injection site: Severe | 0.4 (0.1 to 1.1) | 0 (0.0 to 0.5) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Systemic Events Within 7 Days After Dose 1

| | |
|-----------------|---|
| End point title | Percentage of Subjects With Systemic Events Within 7 Days After Dose 1 ^[5] |
|-----------------|---|

End point description:

Systemic events included fever, decreased appetite, drowsiness/increased sleep, and irritability. Fever was defined as an axillary temperature greater than or equal to (\geq)38.0 degrees Celsius (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). Safety population included all the subjects who received at least 1 dose of the IP with safety follow up after any dose. 'Number of Subjects Analyzed' = number of subjects with any e-diary data reported after Dose 1.

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

End point timeframe:

Within 7 days after Dose 1

Notes:

[5] - 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: Only descriptive data was planned to be analyzed for this endpoint.

| End point values | 20vPnC | 13vPnC | | |
|--|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 993 | 974 | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Fever: \geq 38.0 degree C | 10.3 (8.5 to 12.3) | 7.5 (5.9 to 9.3) | | |
| Fever: \geq 38.0 degree C to 38.4 degree C | 7.3 (5.7 to 9.0) | 6.3 (4.8 to 8.0) | | |
| Fever: >38.4 degree C to 38.9 degree C | 2.2 (1.4 to 3.3) | 0.9 (0.4 to 1.7) | | |
| Fever: >38.9 degree C to 40.0 degree C | 0.7 (0.3 to 1.4) | 0.3 (0.1 to 0.9) | | |
| Fever: >40.0 degree C | 0.1 (0.0 to 0.6) | 0 (0.0 to 0.4) | | |
| Decreased appetite: Any | 24.4 (21.7 to 27.2) | 23.9 (21.3 to 26.7) | | |
| Decreased appetite: Mild | 14.5 (12.4 to 16.8) | 16.1 (13.9 to 18.6) | | |
| Decreased appetite: Moderate | 9.7 (7.9 to 11.7) | 7.5 (5.9 to 9.3) | | |
| Decreased appetite: Severe | 0.2 (0.0 to 0.7) | 0.3 (0.1 to 0.9) | | |
| Drowsiness: Any | 67.2 (64.2 to 70.1) | 66.0 (62.9 to 69.0) | | |
| Drowsiness: Mild | 50.2 (47.0 to 53.3) | 49.3 (46.1 to 52.5) | | |
| Drowsiness: Moderate | 16.1 (13.9 to 18.5) | 15.6 (13.4 to 18.0) | | |

| | | | | |
|---------------------------------------|---------------------|---------------------|--|--|
| Drowsiness: Severe | 0.9 (0.4 to 1.7) | 1.1 (0.6 to 2.0) | | |
| Irritability: Any | 70.9 (68.0 to 73.7) | 71.7 (68.7 to 74.5) | | |
| Irritability: Mild | 23.4 (20.8 to 26.1) | 21.6 (19.0 to 24.3) | | |
| Irritability: Moderate | 43.0 (39.9 to 46.1) | 46.2 (43.0 to 49.4) | | |
| Irritability: Severe | 4.5 (3.3 to 6.0) | 3.9 (2.8 to 5.3) | | |
| Use of antipyretic or pain medication | 35.1 (32.2 to 38.2) | 33.8 (30.8 to 36.8) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Systemic Events Within 7 Days After Dose 2

| | |
|--|---|
| End point title | Percentage of Subjects With Systemic Events Within 7 Days After Dose 2 ^[6] |
| End point description: | |
| Systemic events included fever, decreased appetite, drowsiness/increased sleep, and irritability. Fever was defined as an axillary temperature greater than or equal to (\geq)38.0 degrees 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). Safety population included all the subjects who received at least 1 dose of the IP with safety follow up after any dose. 'Number of Subjects Analyzed' = number of subjects with any e-diary data reported after Dose 2. | |
| End point type | Primary |
| End point timeframe: | |
| Within 7 days after Dose 2 | |

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: Only descriptive data was planned to be analyzed for this endpoint.

| End point values | 20vPnC | 13vPnC | | |
|--|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 940 | 924 | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Fever: \geq 38.0 degree C | 17.3 (15.0 to 19.9) | 16.3 (14.0 to 18.9) | | |
| Fever: \geq 38.0 degree C to 38.4 degree C | 10.9 (8.9 to 13.0) | 10.0 (8.1 to 12.1) | | |
| Fever: >38.4 degree C to 38.9 degree C | 4.0 (2.9 to 5.5) | 4.2 (3.0 to 5.7) | | |
| Fever: >38.9 degree C to 40.0 degree C | 2.2 (1.4 to 3.4) | 2.2 (1.3 to 3.3) | | |
| Fever: >40.0 degree C | 0.2 (0.0 to 0.8) | 0 (0.0 to 0.4) | | |
| Decreased appetite: Any | 26.4 (23.6 to 29.3) | 23.5 (20.8 to 26.4) | | |
| Decreased appetite: Mild | 16.4 (14.1 to 18.9) | 15.3 (13.0 to 17.7) | | |
| Decreased appetite: Moderate | 9.8 (8.0 to 11.9) | 7.7 (6.0 to 9.6) | | |
| Decreased appetite: Severe | 0.2 (0.0 to 0.8) | 0.5 (0.2 to 1.3) | | |

| | | | | |
|---------------------------------------|---------------------|---------------------|--|--|
| Drowsiness: Any | 54.7 (51.4 to 57.9) | 55.6 (52.4 to 58.9) | | |
| Drowsiness: Mild | 37.0 (33.9 to 40.2) | 36.9 (33.8 to 40.1) | | |
| Drowsiness: Moderate | 16.9 (14.6 to 19.5) | 17.9 (15.4 to 20.5) | | |
| Drowsiness: Severe | 0.7 (0.3 to 1.5) | 0.9 (0.4 to 1.7) | | |
| Irritability: Any | 71.6 (68.6 to 74.5) | 68.8 (65.7 to 71.8) | | |
| Irritability: Mild | 22.9 (20.2 to 25.7) | 21.2 (18.6 to 24.0) | | |
| Irritability: Moderate | 44.7 (41.5 to 47.9) | 43.4 (40.2 to 46.7) | | |
| Irritability: Severe | 4.0 (2.9 to 5.5) | 4.2 (3.0 to 5.7) | | |
| Use of antipyretic or pain medication | 40.7 (37.6 to 44.0) | 41.0 (37.8 to 44.3) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Systemic Events Within 7 Days After Dose 3

| | |
|-----------------|---|
| End point title | Percentage of Subjects With Systemic Events Within 7 Days After Dose 3 ^[7] |
|-----------------|---|

End point description:

Systemic events included fever, decreased appetite, drowsiness/increased sleep, and irritability. Fever was defined as an axillary temperature greater than or equal to (\geq)38.0 degrees 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). Safety population included all the subjects who received at least 1 dose of the IP with safety follow up after any dose. 'Number of Subjects Analyzed' = number of subjects with any e-diary data reported after Dose 3.

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

End point timeframe:

Within 7 days after Dose 3

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: Only descriptive data was planned to be analyzed for this endpoint.

| End point values | 20vPnC | 13vPnC | | |
|--|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 914 | 901 | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Fever: \geq 38.0 degree C | 12.6 (10.5 to 14.9) | 13.7 (11.5 to 16.1) | | |
| Fever: \geq 38.0 degree C to 38.4 degree C | 7.7 (6.0 to 9.6) | 7.9 (6.2 to 9.8) | | |
| Fever: >38.4 degree C to 38.9 degree C | 3.4 (2.3 to 4.8) | 3.9 (2.7 to 5.4) | | |
| Fever: >38.9 degree C to 40.0 degree C | 1.4 (0.8 to 2.4) | 1.9 (1.1 to 3.0) | | |
| Fever: >40.0 degree C | 0.1 (0.0 to 0.6) | 0 (0.0 to 0.4) | | |

| | | | | |
|------------------------------------|---------------------|---------------------|--|--|
| Decreased appetite: Any | 20.6 (18.0 to 23.3) | 22.4 (19.7 to 25.3) | | |
| Decreased appetite: Mild | 13.5 (11.3 to 15.8) | 13.9 (11.7 to 16.3) | | |
| Decreased appetite: Moderate | 6.7 (5.1 to 8.5) | 8.2 (6.5 to 10.2) | | |
| Decreased appetite: Severe | 0.4 (0.1 to 1.1) | 0.3 (0.1 to 1.0) | | |
| Drowsiness: Any | 44.1 (40.8 to 47.4) | 44.1 (40.8 to 47.4) | | |
| Drowsiness: Mild | 31.1 (28.1 to 34.2) | 30.1 (27.1 to 33.2) | | |
| Drowsiness: Moderate | 12.5 (10.4 to 14.8) | 13.1 (11.0 to 15.5) | | |
| Drowsiness: Severe | 0.5 (0.2 to 1.3) | 0.9 (0.4 to 1.7) | | |
| Irritability: Any | 64.4 (61.2 to 67.5) | 63.0 (59.8 to 66.2) | | |
| Irritability: Mild | 25.2 (22.4 to 28.1) | 21.6 (19.0 to 24.5) | | |
| Irritability: Moderate | 37.5 (34.4 to 40.8) | 39.2 (36.0 to 42.5) | | |
| Irritability: Severe | 1.8 (1.0 to 2.8) | 2.2 (1.4 to 3.4) | | |
| Use of antipyretic/pain medication | 36.3 (33.2 to 39.5) | 36.1 (32.9 to 39.3) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Systemic Events Within 7 Days After Dose 4

| | |
|-----------------|---|
| End point title | Percentage of Subjects With Systemic Events Within 7 Days After Dose 4 ^[8] |
|-----------------|---|

End point description:

Systemic events included fever, decreased appetite, drowsiness/increased sleep, and irritability. Fever was defined as an axillary temperature greater than or equal to (\geq)38.0 degrees Celsius (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). Safety population included all the subjects who received at least 1 dose of the IP with safety follow up after any dose. 'Number of Subjects Analyzed' = number of subjects with any e-diary data reported after Dose 4.

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

End point timeframe:

Within 7 days after Dose 4

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: Only descriptive data was planned to be analyzed for this endpoint.

| End point values | 20vPnC | 13vPnC | | |
|----------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 826 | 815 | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |

| | | | | |
|--|---------------------|---------------------|--|--|
| Fever: ≥ 38.0 degree C | 14.5 (12.2 to 17.1) | 14.0 (11.7 to 16.6) | | |
| Fever: ≥ 38.0 degree C to 38.4 degree C | 6.5 (4.9 to 8.4) | 7.7 (6.0 to 9.8) | | |
| Fever: >38.4 degree C to 38.9 degree C | 5.1 (3.7 to 6.8) | 3.2 (2.1 to 4.6) | | |
| Fever: >38.9 degree C to 40.0 degree C | 2.7 (1.7 to 4.0) | 2.9 (1.9 to 4.4) | | |
| Fever: >40.0 degree C | 0.2 (0.0 to 0.9) | 0.1 (0.0 to 0.7) | | |
| Decreased appetite: Any | 24.8 (21.9 to 27.9) | 25.2 (22.2 to 28.3) | | |
| Decreased appetite: Mild | 15.9 (13.4 to 18.5) | 16.1 (13.6 to 18.8) | | |
| Decreased appetite: Moderate | 8.6 (6.8 to 10.7) | 8.3 (6.5 to 10.5) | | |
| Decreased appetite: Severe | 0.4 (0.1 to 1.1) | 0.7 (0.3 to 1.6) | | |
| Drowsiness: Any | 39.5 (36.1 to 42.9) | 39.5 (36.1 to 43.0) | | |
| Drowsiness: Mild | 27.8 (24.8 to 31.0) | 28.2 (25.2 to 31.4) | | |
| Drowsiness: Moderate | 11.0 (9.0 to 13.4) | 10.7 (8.6 to 13.0) | | |
| Drowsiness: Severe | 0.6 (0.2 to 1.4) | 0.6 (0.2 to 1.4) | | |
| Irritability: Any | 61.0 (57.6 to 64.4) | 61.1 (57.7 to 64.5) | | |
| Irritability: Mild | 23.4 (20.5 to 26.4) | 21.8 (19.0 to 24.8) | | |
| Irritability: Moderate | 35.0 (31.7 to 38.3) | 37.9 (34.6 to 41.3) | | |
| Irritability: Severe | 2.7 (1.7 to 4.0) | 1.3 (0.7 to 2.4) | | |
| Use of antipyretic/pain medication | 37.5 (34.2 to 40.9) | 36.7 (33.4 to 40.1) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Adverse Events (AEs) From Dose 1 to 1 Month After Dose 3

| | |
|-----------------|---|
| End point title | Percentage of Subjects With Adverse Events (AEs) From Dose 1 to 1 Month After Dose 3 ^[9] |
|-----------------|---|

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. Safety population included all the subjects who received at least 1 dose of the IP with safety follow up after any dose. Here, 'Number of Subjects Analyzed' = number of subjects who received Dose 1.

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

End point timeframe:

From Dose 1 to 1 Month after Dose 3

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: Only descriptive data was planned to be analyzed for this endpoint.

| End point values | 20vPnC | 13vPnC | | |
|----------------------------------|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1001 | 987 | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | 36.6 (33.6 to 39.6) | 39.4 (36.3 to 42.5) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With AEs from Dose 4 to 1 Month After Dose 4

| | |
|-----------------|---|
| End point title | Percentage of Subjects With AEs from Dose 4 to 1 Month After Dose 4 ^[10] |
|-----------------|---|

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. Safety population included all the subjects who received at least 1 dose of the IP with safety follow up after any dose. Here, 'Number of Subjects Analyzed' = number of subjects who received Dose 4 and had safety follow up after Dose 4.

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

End point timeframe:

From Dose 4 to 1 month after Dose 4

Notes:

[10] - 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: Only descriptive data was planned to be analyzed for this endpoint.

| End point values | 20vPnC | 13vPnC | | |
|----------------------------------|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 853 | 841 | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | 15.1 (12.8 to 17.7) | 15.0 (12.6 to 17.6) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Serious Adverse Events (SAEs) From Dose 1 to 6 Months Following Dose 4

| | |
|-----------------|--|
| End point title | Percentage of Subjects With Serious Adverse Events (SAEs) From Dose 1 to 6 Months Following Dose 4 ^[11] |
|-----------------|--|

End point description:

A SAE was any untoward medical occurrence that, at any dose: resulted in death; required inpatient hospitalisation or prolongation of existing hospitalisation; was life-threatening; resulted in persistent or significant disability/ incapacity; congenital anomaly/birth defect and other important medical events. Safety population included all the subjects who received at least 1 dose of the IP with safety follow up after any dose. Here, 'Number of Subjects Analyzed' = number of subjects who received Dose 1.

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

End point timeframe:

From Dose 1 to 6 months following Dose 4

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: Only descriptive data was planned to be analyzed for this endpoint.

| End point values | 20vPnC | 13vPnC | | |
|----------------------------------|------------------|------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1001 | 987 | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | 4.5 (3.3 to 6.0) | 3.1 (2.1 to 4.4) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Newly Diagnosed Chronic Medical Conditions (NDCMCs) From Dose 1 to 6 Months Following Dose 4

| | |
|-----------------|--|
| End point title | Percentage of Subjects With Newly Diagnosed Chronic Medical Conditions (NDCMCs) From Dose 1 to 6 Months Following Dose 4 ^[12] |
|-----------------|--|

End point description:

An NDCMC was defined as a significant disease or medical condition, not previously identified, that was expected to be persistent or was otherwise long-lasting in its effects. Safety population included all the subjects who received at least 1 dose of the IP with safety follow up after any dose. Here, 'Number of Subjects Analyzed' = number of subjects who received Dose 1.

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

End point timeframe:

From Dose 1 to 6 months following Dose 4

Notes:

[12] - 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: Only descriptive data was planned to be analyzed for this endpoint.

| End point values | 20vPnC | 13vPnC | | |
|----------------------------------|------------------|------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1001 | 987 | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | 5.0 (3.7 to 6.5) | 5.9 (4.5 to 7.5) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Predefined Serotype-specific Immunoglobulin G (IgG) Concentrations 1 Month After Dose 3

| | |
|-----------------|---|
| End point title | Percentage of Subjects With Predefined Serotype-specific Immunoglobulin G (IgG) Concentrations 1 Month After Dose 3 |
|-----------------|---|

End point description:

Pre-specified levels of serotypes were as follows: for serotype 1, 3, 4, 6A, 7F, 9V, 14, 18C, 19F, 23F, 8, 10A, 11A, 12F, 15B, 22F, 33F: ≥ 0.35 microgram per mL (mcg/mL), for serotype 5: ≥ 0.23 mcg/mL, for serotype 6B: ≥ 0.10 mcg/mL and for serotype 19A: ≥ 0.12 mcg/mL. "Numbers of Subjects Analyzed" were the denominators and numbers of participants with an IgG concentration \geq the predefined level for the given serotype were the numerator for the percentage calculations. 95% CI was based on the Clopper and Pearson method. Dose 3 evaluable population: eligible subjects aged 42-98 days on Dose 1, received the first 3 doses to which they were randomized, have at least 1 valid immunogenicity result within 27 to 56 days post Dose 3, and had no other major protocol deviations as determined by the clinician. Here, "Number of Subjects Analyzed" = number of participants with valid IgG concentrations for the specified serotype reported at 1 month after Dose 3.

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

End point timeframe:

1 month after Dose 3

| End point values | 20vPnC | 13vPnC | | |
|----------------------------------|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 833 | 803 | | |
| Units: percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Serotype 1 (n=833, 802) | 79.8 (76.9 to 82.5) | 88.4 (86.0 to 90.5) | | |
| Serotype 3 (n=833, 802) | 52.1 (48.6 to 55.5) | 67.6 (64.2 to 70.8) | | |
| Serotype 4 (n=833, 802) | 79.7 (76.8 to 82.4) | 88.2 (85.7 to 90.3) | | |
| Serotype 5 (n=833, 802) | 82.5 (79.7 to 85.0) | 86.8 (84.2 to 89.1) | | |
| Serotype 6A (n=833, 802) | 93.5 (91.6 to 95.1) | 95.9 (94.3 to 97.2) | | |
| Serotype 6B (n=831, 801) | 88.3 (85.9 to 90.4) | 92.4 (90.3 to 94.1) | | |
| Serotype 7F (n=833, 802) | 96.6 (95.2 to 97.8) | 97.6 (96.3 to 98.6) | | |
| Serotype 9V (n=833, 802) | 81.9 (79.1 to 84.4) | 89.8 (87.5 to 91.8) | | |
| Serotype 14 (n=832, 802) | 93.4 (91.5 to 95.0) | 94.1 (92.3 to 95.7) | | |
| Serotype 18C (n=833, 802) | 92.6 (90.6 to 94.2) | 93.1 (91.2 to 94.8) | | |
| Serotype 19A (n=833, 802) | 97.1 (95.7 to 98.1) | 98.1 (96.9 to 98.9) | | |
| Serotype 19F (n=833, 802) | 96.9 (95.5 to 98.0) | 96.6 (95.1 to 97.8) | | |
| Serotype 23F (n=833, 802) | 77.9 (74.9 to 80.7) | 85.5 (82.9 to 87.9) | | |
| Serotype 8 (n=833, 794) | 96.8 (95.3 to 97.9) | 1.6 (0.9 to 2.8) | | |
| Serotype 10A (n=833, 803) | 82.2 (79.5 to 84.8) | 1.2 (0.6 to 2.3) | | |
| Serotype 11A (n=833, 803) | 92.7 (90.7 to 94.4) | 1.5 (0.8 to 2.6) | | |
| Serotype 12F (n=833, 803) | 67.5 (64.2 to 70.6) | 0.1 (0.0 to 0.7) | | |
| Serotype 15B (n=833, 803) | 98.2 (97.0 to 99.0) | 2.6 (1.6 to 4.0) | | |

| | | | | |
|---------------------------|---------------------|------------------|--|--|
| Serotype 22F (n=833, 803) | 98.3 (97.2 to 99.1) | 0.9 (0.4 to 1.8) | | |
| Serotype 33F (n=833, 802) | 86.7 (84.2 to 88.9) | 1.1 (0.5 to 2.1) | | |

Statistical analyses

| | |
|--|--|
| Statistical analysis title | NI of 20vPnC-13vPnC for matched serotype |
| Statistical analysis description: | |
| Serotype 1: 2-Sided CI were calculated based on the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage | |
| Comparison groups | 20vPnC v 13vPnC |
| Number of subjects included in analysis | 1636 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[13] |
| Parameter estimate | percentage difference |
| Point estimate | -8.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -12.1 |
| upper limit | -5.1 |

Notes:

[13] - Comparison was conducted for the 13 matched serotypes for 20vPnC to the corresponding serotype in 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the percentage differences (20vPnC - 13vPnC) was greater than -10%.

| | |
|--|---|
| Statistical analysis title | NI of 20vPnC-13vPnC for 13 matched serotype |
| Statistical analysis description: | |
| Serotype 4: 2-Sided CI were calculated based on the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage | |
| Comparison groups | 20vPnC v 13vPnC |
| Number of subjects included in analysis | 1636 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[14] |
| Parameter estimate | percentage difference |
| Point estimate | -8.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -12 |
| upper limit | -4.9 |

Notes:

[14] - Comparison was conducted for the 13 matched serotypes for 20vPnC to the corresponding serotype in 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the percentage differences (20vPnC - 13vPnC) was greater than -10%.

| | |
|--|---|
| Statistical analysis title | NI of 20vPnC-13vPnC for 13 matched serotype |
| Statistical analysis description: | |
| Serotype 3: 2-Sided CI were calculated based on the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage | |
| Comparison groups | 20vPnC v 13vPnC |

| | |
|---|---------------------------------|
| Number of subjects included in analysis | 1636 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[15] |
| Parameter estimate | percentage difference |
| Point estimate | -15.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -20.1 |
| upper limit | -10.8 |

Notes:

[15] - Comparison was conducted for the 13 matched serotypes for 20vPnC to the corresponding serotype in 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the percentage differences (20vPnC - 13vPnC) was greater than -10%.

| | |
|-----------------------------------|---|
| Statistical analysis title | NI of 20vPnC-13vPnC for 13 matched serotype |
|-----------------------------------|---|

Statistical analysis description:

Serotype 5: 2-Sided CI were calculated based on the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage

| | |
|---|---------------------------------|
| Comparison groups | 20vPnC v 13vPnC |
| Number of subjects included in analysis | 1636 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[16] |
| Parameter estimate | percentage difference |
| Point estimate | -4.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -7.8 |
| upper limit | -0.8 |

Notes:

[16] - Comparison was conducted for the 13 matched serotypes for 20vPnC to the corresponding serotype in 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the percentage differences (20vPnC - 13vPnC) was greater than -10%.

| | |
|-----------------------------------|---|
| Statistical analysis title | NI of 20vPnC-13vPnC for 13 matched serotype |
|-----------------------------------|---|

Statistical analysis description:

Serotype 6A: 2-Sided CI were calculated based on the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage

| | |
|---|---------------------------------|
| Comparison groups | 20vPnC v 13vPnC |
| Number of subjects included in analysis | 1636 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[17] |
| Parameter estimate | percentage difference |
| Point estimate | -2.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -4.6 |
| upper limit | -0.2 |

Notes:

[17] - Comparison was conducted for the 13 matched serotypes for 20vPnC to the corresponding serotype in 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the percentage differences (20vPnC - 13vPnC) was greater than -10%.

| | |
|---|---|
| Statistical analysis title | NI of 20vPnC-13vPnC for 13 matched serotype |
| Statistical analysis description: | |
| Serotype 6B: 2-Sided CI were calculated based on the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage | |
| Comparison groups | 20vPnC v 13vPnC |
| Number of subjects included in analysis | 1636 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[18] |
| Parameter estimate | percentage difference |
| Point estimate | -4.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -7 |
| upper limit | -1.2 |

Notes:

[18] - Comparison was conducted for the 13 matched serotypes for 20vPnC to the corresponding serotype in 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the percentage differences (20vPnC - 13vPnC) was greater than -10%.

| | |
|---|---|
| Statistical analysis title | NI of 20vPnC-13vPnC for 13 matched serotype |
| Statistical analysis description: | |
| Serotype 14: 2-Sided CI were calculated based on the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage | |
| Comparison groups | 20vPnC v 13vPnC |
| Number of subjects included in analysis | 1636 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[19] |
| Parameter estimate | percentage difference |
| Point estimate | -0.8 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.1 |
| upper limit | 1.6 |

Notes:

[19] - Comparison was conducted for the 13 matched serotypes for 20vPnC to the corresponding serotype in 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the percentage differences (20vPnC - 13vPnC) was greater than -10%.

| | |
|---|---|
| Statistical analysis title | NI of 20vPnC-13vPnC for 13 matched serotype |
| Statistical analysis description: | |
| Serotype 9V: 2-Sided CI were calculated based on the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage | |
| Comparison groups | 20vPnC v 13vPnC |
| Number of subjects included in analysis | 1636 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[20] |
| Parameter estimate | percentage difference |
| Point estimate | -7.9 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -11.3 |
| upper limit | -4.6 |

Notes:

[20] - Comparison was conducted for the 13 matched serotypes for 20vPnC to the corresponding serotype in 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the percentage differences (20vPnC - 13vPnC) was greater than -10%.

| | |
|-----------------------------------|---|
| Statistical analysis title | NI of 20vPnC-13vPnC for 13 matched serotype |
|-----------------------------------|---|

Statistical analysis description:

Serotype 7F: 2-sided CI were calculated based on the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage

| | |
|---|---------------------------------|
| Comparison groups | 20vPnC v 13vPnC |
| Number of subjects included in analysis | 1636 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[21] |
| Parameter estimate | percentage difference |
| Point estimate | -1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.7 |
| upper limit | 0.7 |

Notes:

[21] - Comparison was conducted for the 13 matched serotypes for 20vPnC to the corresponding serotype in 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the percentage differences (20vPnC - 13vPnC) was greater than -10%.

| | |
|-----------------------------------|---|
| Statistical analysis title | NI of 20vPnC-13vPnC for 13 matched serotype |
|-----------------------------------|---|

Statistical analysis description:

Serotype 18C: 2-Sided CI were calculated based on the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage

| | |
|---|---------------------------------|
| Comparison groups | 20vPnC v 13vPnC |
| Number of subjects included in analysis | 1636 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[22] |
| Parameter estimate | percentage difference |
| Point estimate | -0.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.1 |
| upper limit | 1.9 |

Notes:

[22] - Comparison was conducted for the 13 matched serotypes for 20vPnC to the corresponding serotype in 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the percentage differences (20vPnC - 13vPnC) was greater than -10%.

| | |
|-----------------------------------|---|
| Statistical analysis title | NI of 20vPnC-13vPnC for 13 matched serotype |
|-----------------------------------|---|

Statistical analysis description:

Serotype 19F: 2-Sided CI were calculated based on the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage

| | |
|-------------------|-----------------|
| Comparison groups | 20vPnC v 13vPnC |
|-------------------|-----------------|

| | |
|---|---------------------------------|
| Number of subjects included in analysis | 1636 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[23] |
| Parameter estimate | percentage difference |
| Point estimate | 0.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.5 |
| upper limit | 2 |

Notes:

[23] - Comparison was conducted for the 13 matched serotypes for 20vPnC to the corresponding serotype in 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the percentage differences (20vPnC - 13vPnC) was greater than -10%.

| | |
|-----------------------------------|---|
| Statistical analysis title | NI of 20vPnC-13vPnC for 13 matched serotype |
|-----------------------------------|---|

Statistical analysis description:

Serotype 19A: 2-Sided CI were calculated based on the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage

| | |
|---|---------------------------------|
| Comparison groups | 20vPnC v 13vPnC |
| Number of subjects included in analysis | 1636 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[24] |
| Parameter estimate | percentage difference |
| Point estimate | -1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.6 |
| upper limit | 0.5 |

Notes:

[24] - Comparison was conducted for the 13 matched serotypes for 20vPnC to the corresponding serotype in 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the percentage differences (20vPnC - 13vPnC) was greater than -10%.

| | |
|-----------------------------------|---|
| Statistical analysis title | NI of 20vPnC-13vPnC for 13 matched serotype |
|-----------------------------------|---|

Statistical analysis description:

Serotype 23F: 2-Sided CI were calculated based on the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage

| | |
|---|---------------------------------|
| Comparison groups | 20vPnC v 13vPnC |
| Number of subjects included in analysis | 1636 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[25] |
| Parameter estimate | percentage difference |
| Point estimate | -7.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -11.4 |
| upper limit | -3.9 |

Notes:

[25] - Comparison was conducted for the 13 matched serotypes for 20vPnC to the corresponding serotype in 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the percentage differences (20vPnC - 13vPnC) was greater than -10%.

| | |
|--|---|
| Statistical analysis title | NI of 20vPnC - 13vPnC for 7 additional serotype |
| Statistical analysis description: | |
| Serotype 8: 2-Sided CI were calculated based on the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage | |
| Comparison groups | 20vPnC v 13vPnC |
| Number of subjects included in analysis | 1636 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[26] |
| Parameter estimate | percentage difference |
| Point estimate | 11.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 8.6 |
| upper limit | 14 |

Notes:

[26] - For the additional 7 serotypes, the compared results were from serotype 23F (13vPnC serotype with the lowest percentage, not including serotype 3) in the 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the percentage differences (20vPnC - lowest 13vPnC) was greater than -10%.

| | |
|--|---|
| Statistical analysis title | NI of 20vPnC - 13vPnC for 7 additional serotype |
| Statistical analysis description: | |
| Serotype 10A: 2-Sided CI were calculated based on the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage | |
| Comparison groups | 20vPnC v 13vPnC |
| Number of subjects included in analysis | 1636 |
| Analysis specification | Pre-specified |
| Analysis type | other ^[27] |
| Parameter estimate | percentage difference |
| Point estimate | -3.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -6.9 |
| upper limit | 0.3 |

Notes:

[27] - For the additional 7 serotypes, the compared results were from serotype 23F (13vPnC serotype with the lowest percentage, not including serotype 3) in the 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the percentage differences (20vPnC - lowest 13vPnC) was greater than -10%.

| | |
|--|---|
| Statistical analysis title | NI of 20vPnC - 13vPnC for 7 additional serotype |
| Statistical analysis description: | |
| Serotype 11A: 2-Sided CI were calculated based on the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage | |
| Comparison groups | 20vPnC v 13vPnC |
| Number of subjects included in analysis | 1636 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[28] |
| Parameter estimate | percentage difference |
| Point estimate | 7.1 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 4.2 |
| upper limit | 10.2 |

Notes:

[28] - For the additional 7 serotypes, the compared results were from serotype 23F (13vPnC serotype with the lowest percentage, not including serotype 3) in the 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the percentage differences (20vPnC - lowest 13vPnC) was greater than -10%.

| | |
|-----------------------------------|---|
| Statistical analysis title | NI of 20vPnC - 13vPnC for 7 additional serotype |
|-----------------------------------|---|

Statistical analysis description:

Serotype 12F: 2-Sided CI were calculated based on the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage

| | |
|---|---------------------------------|
| Comparison groups | 20vPnC v 13vPnC |
| Number of subjects included in analysis | 1636 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[29] |
| Parameter estimate | percentage difference |
| Point estimate | -18.1 |

Confidence interval

| | |
|-------------|---------|
| level | 95 % |
| sides | 2-sided |
| lower limit | -22.1 |
| upper limit | -14 |

Notes:

[29] - For the additional 7 serotypes, the compared results were from serotype 23F (13vPnC serotype with the lowest percentage, not including serotype 3) in the 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the percentage differences (20vPnC - lowest 13vPnC) was greater than -10%.

| | |
|-----------------------------------|---|
| Statistical analysis title | NI of 20vPnC - 13vPnC for 7 additional serotype |
|-----------------------------------|---|

Statistical analysis description:

Serotype 22F: 2-Sided CI were calculated based on the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage

| | |
|---|---------------------------------|
| Comparison groups | 20vPnC v 13vPnC |
| Number of subjects included in analysis | 1636 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[30] |
| Parameter estimate | percentage difference |
| Point estimate | 12.8 |

Confidence interval

| | |
|-------------|---------|
| level | 95 % |
| sides | 2-sided |
| lower limit | 10.3 |
| upper limit | 15.5 |

Notes:

[30] - For the additional 7 serotypes, the compared results were from serotype 23F (13vPnC serotype with the lowest percentage, not including serotype 3) in the 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the percentage differences (20vPnC - lowest 13vPnC) was greater than -10%.

| | |
|-----------------------------------|---|
| Statistical analysis title | NI of 20vPnC - 13vPnC for 7 additional serotype |
|-----------------------------------|---|

Statistical analysis description:

Serotype 15B: 2-Sided CI were calculated based on the Miettinen and Nurminen method for the

difference in proportions, expressed as a percentage

| | |
|---|---------------------------------|
| Comparison groups | 20vPnC v 13vPnC |
| Number of subjects included in analysis | 1636 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[31] |
| Parameter estimate | percentage difference |
| Point estimate | 12.7 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 10.2 |
| upper limit | 15.4 |

Notes:

[31] - For the additional 7 serotypes, the compared results were from serotype 23F (13vPnC serotype with the lowest percentage, not including serotype 3) in the 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the percentage differences (20vPnC - lowest 13vPnC) was greater than -10%.

| | |
|-----------------------------------|---|
| Statistical analysis title | NI of 20vPnC - 13vPnC for 7 additional serotype |
|-----------------------------------|---|

Statistical analysis description:

Serotype 33F: 2-Sided CI were calculated based on the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage

| | |
|---|---------------------------------|
| Comparison groups | 20vPnC v 13vPnC |
| Number of subjects included in analysis | 1636 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[32] |
| Parameter estimate | percentage difference |
| Point estimate | 1.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.2 |
| upper limit | 4.5 |

Notes:

[32] - For the additional 7 serotypes, the compared results were from serotype 23F (13vPnC serotype with the lowest percentage, not including serotype 3) in the 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the percentage differences (20vPnC - lowest 13vPnC) was greater than -10%.

Primary: Serotype-specific IgG Geometric Mean Concentrations (GMCs) and Geometric Mean Ratios (GMRs) at 1 Month After Dose 4

| | |
|-----------------|---|
| End point title | Serotype-specific IgG Geometric Mean Concentrations (GMCs) and Geometric Mean Ratios (GMRs) at 1 Month After Dose 4 |
|-----------------|---|

End point description:

Concentrations of anticapsular IgG for the 20 pneumococcal serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F, 8, 10A, 11A, 12F, 15B, 22F, and 33F) were determined in all subjects at 1 month after Dose 4 using the Luminex assay. Results were expressed as IgG concentrations. GMCs and 2-sided CIs were calculated by exponentiating the mean logarithm of the concentrations and the corresponding CIs based on the Student's t distribution. Dose 4 evaluable immunogenicity population: eligible subjects aged 42-98 days on Dose 1, received all 4 doses to which they were randomized, and were 365 to 455 days of age, inclusive, on the day of Dose 4, had at least 1 valid immunogenicity result within 27 to 56 days after Dose 4, and had no other major protocol deviations as determined by the clinician. Here, "Number of Subjects Analyzed" = number of participants with valid IgG concentrations for the specified serotype reported at 1 month after Dose 4.

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

End point timeframe:

1 month after Dose 4

| End point values | 20vPnC | 13vPnC | | |
|--|------------------------|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 755 | 745 | | |
| Units: microgram per milliliter (µg/mL) | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Serotype 1 (n=755, 744) | 1.47 (1.37 to 1.57) | 2.12 (1.97 to 2.27) | | |
| Serotype 3 (n=755, 745) | 0.56 (0.53 to 0.60) | 0.85 (0.80 to 0.90) | | |
| Serotype 4 (n=754, 745) | 3.77 (3.52 to 4.04) | 4.84 (4.50 to 5.22) | | |
| Serotype 5 (n=755, 745) | 1.87 (1.74 to 2.00) | 2.51 (2.33 to 2.70) | | |
| Serotype 6A (n=755, 745) | 9.01 (8.45 to 9.61) | 11.69 (10.91 to 12.53) | | |
| Serotype 6B (n=753, 744) | 4.01 (3.70 to 4.35) | 5.74 (5.27 to 6.24) | | |
| Serotype 7F (n=755, 745) | 3.91 (3.70 to 4.14) | 5.18 (4.88 to 5.49) | | |
| Serotype 9V (n=755, 744) | 3.44 (3.23 to 3.67) | 4.30 (4.02 to 4.59) | | |
| Serotype 14 (n=755, 745) | 5.68 (5.27 to 6.12) | 6.34 (5.88 to 6.83) | | |
| Serotype 18C (n=755, 745) | 3.46 (3.24 to 3.70) | 4.69 (4.34 to 5.05) | | |
| Serotype 19A (n=754, 745) | 3.53 (3.30 to 3.77) | 4.13 (3.84 to 4.45) | | |
| Serotype 19F (n=755, 745) | 5.01 (4.68 to 5.36) | 5.79 (5.36 to 6.25) | | |
| Serotype 23F (n=755, 745) | 3.95 (3.63 to 4.31) | 6.18 (5.66 to 6.75) | | |
| Serotype 8 (n=755, 720) | 3.97 (3.73 to 4.22) | 0.03 (0.03 to 0.04) | | |
| Serotype 10A (n=755, 744) | 6.22 (5.75 to 6.72) | 0.01 (0.01 to 0.01) | | |
| Serotype 11A (n=755, 745) | 3.53 (3.31 to 3.78) | 0.02 (0.02 to 0.02) | | |
| Serotype 12F (n=755, 745) | 1.85 (1.73 to 1.99) | 0.01 (0.01 to 0.01) | | |
| Serotype 15B (n=755, 745) | 12.59 (11.78 to 13.45) | 0.02 (0.02 to 0.03) | | |
| Serotype 22F (n=755, 745) | 10.60 (9.92 to 11.33) | 0.00 (0.00 to 0.01) | | |
| Serotype 33F (n=755, 745) | 9.31 (8.71 to 9.96) | 0.01 (0.01 to 0.01) | | |

Statistical analyses

| Statistical analysis title | NI of 20vPnC-13vPnC for 13 matched serotype |
|-----------------------------------|---|
|-----------------------------------|---|

Statistical analysis description:

Serotype 5: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC-

13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution).

| | |
|---|---------------------------------|
| Comparison groups | 20vPnC v 13vPnC |
| Number of subjects included in analysis | 1500 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[33] |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 0.74 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.67 |
| upper limit | 0.82 |

Notes:

[33] - Comparison for the 13 matched serotypes for 20vPnC was to the corresponding serotype in 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the IgG GMR of 20vPnC to 13vPnC for the serotype is greater than 0.5 (2-fold NI margin).

| | |
|-----------------------------------|---|
| Statistical analysis title | NI of 20vPnC-13vPnC for 13 matched serotype |
|-----------------------------------|---|

Statistical analysis description:

Serotype 4: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC-13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution).

| | |
|---|---------------------------------|
| Comparison groups | 20vPnC v 13vPnC |
| Number of subjects included in analysis | 1500 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[34] |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 0.78 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.7 |
| upper limit | 0.86 |

Notes:

[34] - Comparison for the 13 matched serotypes for 20vPnC was to the corresponding serotype in 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the IgG GMR of 20vPnC to 13vPnC for the serotype is greater than 0.5 (2-fold NI margin).

| | |
|-----------------------------------|---|
| Statistical analysis title | NI of 20vPnC-13vPnC for 13 matched serotype |
|-----------------------------------|---|

Statistical analysis description:

Serotype 3: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC-13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution).

| | |
|---|---------------------------------|
| Comparison groups | 20vPnC v 13vPnC |
| Number of subjects included in analysis | 1500 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[35] |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 0.66 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.61 |
| upper limit | 0.73 |

Notes:

[35] - Comparison for the 13 matched serotypes for 20vPnC was to the corresponding serotype in 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the IgG GMR of 20vPnC to 13vPnC for the serotype is greater than 0.5 (2-fold NI margin).

| | |
|--|---|
| Statistical analysis title | NI of 20vPnC-13vPnC for 13 matched serotype |
| Statistical analysis description: | |
| Serotype 1: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC-13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution). | |
| Comparison groups | 20vPnC v 13vPnC |
| Number of subjects included in analysis | 1500 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[36] |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 0.69 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.63 |
| upper limit | 0.76 |

Notes:

[36] - Comparison for the 13 matched serotypes for 20vPnC was to the corresponding serotype in 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the IgG GMR of 20vPnC to 13vPnC for the serotype is greater than 0.5 (2-fold NI margin).

| | |
|---|---|
| Statistical analysis title | NI of 20vPnC-13vPnC for 13 matched serotype |
| Statistical analysis description: | |
| Serotype 6A: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC-13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution). | |
| Comparison groups | 20vPnC v 13vPnC |
| Number of subjects included in analysis | 1500 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[37] |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 0.77 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.7 |
| upper limit | 0.85 |

Notes:

[37] - Comparison for the 13 matched serotypes for 20vPnC was to the corresponding serotype in 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the IgG GMR of 20vPnC to 13vPnC for the serotype is greater than 0.5 (2-fold NI margin).

| | |
|---|---|
| Statistical analysis title | NI of 20vPnC-13vPnC for 13 matched serotype |
| Statistical analysis description: | |
| Serotype 14: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC-13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution). | |
| Comparison groups | 20vPnC v 13vPnC |

| | |
|---|---------------------------------|
| Number of subjects included in analysis | 1500 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[38] |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 0.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.81 |
| upper limit | 1 |

Notes:

[38] - Comparison for the 13 matched serotypes for 20vPnC was to the corresponding serotype in 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the IgG GMR of 20vPnC to 13vPnC for the serotype is greater than 0.5 (2-fold NI margin).

| | |
|-----------------------------------|---|
| Statistical analysis title | NI of 20vPnC-13vPnC for 13 matched serotype |
|-----------------------------------|---|

Statistical analysis description:

Serotype 9V: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC-13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution).

| | |
|---|---------------------------------|
| Comparison groups | 20vPnC v 13vPnC |
| Number of subjects included in analysis | 1500 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[39] |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 0.8 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.73 |
| upper limit | 0.88 |

Notes:

[39] - Comparison for the 13 matched serotypes for 20vPnC was to the corresponding serotype in 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the IgG GMR of 20vPnC to 13vPnC for the serotype is greater than 0.5 (2-fold NI margin).

| | |
|-----------------------------------|---|
| Statistical analysis title | NI of 20vPnC-13vPnC for 13 matched serotype |
|-----------------------------------|---|

Statistical analysis description:

Serotype 7F: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC-13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution).

| | |
|---|---------------------------------|
| Comparison groups | 20vPnC v 13vPnC |
| Number of subjects included in analysis | 1500 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[40] |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 0.76 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.7 |
| upper limit | 0.82 |

Notes:

[40] - Comparison for the 13 matched serotypes for 20vPnC was to the corresponding serotype in 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the IgG GMR of 20vPnC to 13vPnC for the serotype is greater than 0.5 (2-fold NI margin).

| | |
|--|---|
| Statistical analysis title | NI of 20vPnC-13vPnC for 13 matched serotype |
| Statistical analysis description: Serotype 6B: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC-13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution). | |
| Comparison groups | 20vPnC v 13vPnC |
| Number of subjects included in analysis | 1500 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[41] |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 0.7 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.62 |
| upper limit | 0.79 |

Notes:

[41] - Comparison for the 13 matched serotypes for 20vPnC was to the corresponding serotype in 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the IgG GMR of 20vPnC to 13vPnC for the serotype is greater than 0.5 (2-fold NI margin).

| | |
|---|---|
| Statistical analysis title | NI of 20vPnC-13vPnC for 13 matched serotype |
| Statistical analysis description: Serotype 18C: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC-13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution). | |
| Comparison groups | 20vPnC v 13vPnC |
| Number of subjects included in analysis | 1500 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[42] |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 0.74 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.67 |
| upper limit | 0.82 |

Notes:

[42] - Comparison for the 13 matched serotypes for 20vPnC was to the corresponding serotype in 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the IgG GMR of 20vPnC to 13vPnC for the serotype is greater than 0.5 (2-fold NI margin).

| | |
|--|---|
| Statistical analysis title | NI of 20vPnC - 13vPnC for 7 additional serotype |
| Statistical analysis description: Serotype 10A: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC - lowest 13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution). | |
| Comparison groups | 20vPnC v 13vPnC |

| | |
|---|---------------------------------|
| Number of subjects included in analysis | 1500 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[43] |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 2.94 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 2.64 |
| upper limit | 3.26 |

Notes:

[43] - For the additional 7 serotypes, the compared results were from serotype 1 (13vPnC serotype with the lowest GMC, not including serotype 3) in the 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the GMR (20vPnC/lowest 13vPnC) was greater than 0.5 (2-fold criterion).

| | |
|-----------------------------------|---|
| Statistical analysis title | NI of 20vPnC - 13vPnC for 7 additional serotype |
|-----------------------------------|---|

Statistical analysis description:

Serotype 8: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC - lowest 13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution).

| | |
|---|---------------------------------|
| Comparison groups | 20vPnC v 13vPnC |
| Number of subjects included in analysis | 1500 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[44] |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 1.87 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.71 |
| upper limit | 2.06 |

Notes:

[44] - For the additional 7 serotypes, the compared results were from serotype 1 (13vPnC serotype with the lowest GMC, not including serotype 3) in the 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the GMR (20vPnC/lowest 13vPnC) was greater than 0.5 (2-fold criterion).

| | |
|-----------------------------------|---|
| Statistical analysis title | NI of 20vPnC-13vPnC for 13 matched serotype |
|-----------------------------------|---|

Statistical analysis description:

Serotype 23F: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC-13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution).

| | |
|---|---------------------------------|
| Comparison groups | 20vPnC v 13vPnC |
| Number of subjects included in analysis | 1500 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[45] |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 0.64 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.57 |
| upper limit | 0.72 |

Notes:

[45] - Comparison for the 13 matched serotypes for 20vPnC was to the corresponding serotype in 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the IgG GMR of 20vPnC to 13vPnC for the serotype is greater than 0.5 (2-fold NI margin).

| | |
|---|---|
| Statistical analysis title | NI of 20vPnC-13vPnC for 13 matched serotype |
| Statistical analysis description: Serotype 19F: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC-13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution). | |
| Comparison groups | 20vPnC v 13vPnC |
| Number of subjects included in analysis | 1500 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[46] |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 0.86 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.78 |
| upper limit | 0.96 |

Notes:

[46] - Comparison for the 13 matched serotypes for 20vPnC was to the corresponding serotype in 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the IgG GMR of 20vPnC to 13vPnC for the serotype is greater than 0.5 (2-fold NI margin).

| | |
|---|---|
| Statistical analysis title | NI of 20vPnC-13vPnC for 13 matched serotype |
| Statistical analysis description: Serotype 19A: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC-13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution). | |
| Comparison groups | 20vPnC v 13vPnC |
| Number of subjects included in analysis | 1500 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[47] |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 0.85 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.77 |
| upper limit | 0.94 |

Notes:

[47] - Comparison for the 13 matched serotypes for 20vPnC was to the corresponding serotype in 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the IgG GMR of 20vPnC to 13vPnC for the serotype is greater than 0.5 (2-fold NI margin).

| | |
|--|---|
| Statistical analysis title | NI of 20vPnC - 13vPnC for 7 additional serotype |
| Statistical analysis description: Serotype 15B: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC - lowest 13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution). | |
| Comparison groups | 20vPnC v 13vPnC |

| | |
|---|---------------------------------|
| Number of subjects included in analysis | 1500 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[48] |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 5.95 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 5.39 |
| upper limit | 6.55 |

Notes:

[48] - For the additional 7 serotypes, the compared results were from serotype 5 (13vPnC serotype with the lowest GMC, not including serotype 3) in the 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the GMR (20vPnC/lowest 13vPnC) was greater than 0.5 (2-fold criterion).

| | |
|-----------------------------------|---|
| Statistical analysis title | NI of 20vPnC - 13vPnC for 7 additional serotype |
|-----------------------------------|---|

Statistical analysis description:

Serotype 12F: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC - lowest 13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution).

| | |
|---|---------------------------------|
| Comparison groups | 20vPnC v 13vPnC |
| Number of subjects included in analysis | 1500 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[49] |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 0.88 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.79 |
| upper limit | 0.97 |

Notes:

[49] - For the additional 7 serotypes, the compared results were from serotype 5 (13vPnC serotype with the lowest GMC, not including serotype 3) in the 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the GMR (20vPnC/lowest 13vPnC) was greater than 0.5 (2-fold criterion).

| | |
|-----------------------------------|---|
| Statistical analysis title | NI of 20vPnC - 13vPnC for 7 additional serotype |
|-----------------------------------|---|

Statistical analysis description:

Serotype 11A: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC - lowest 13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution).

| | |
|---|---------------------------------|
| Comparison groups | 20vPnC v 13vPnC |
| Number of subjects included in analysis | 1500 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[50] |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 1.67 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.51 |
| upper limit | 1.84 |

Notes:

[50] - For the additional 7 serotypes, the compared results were from serotype 5 (13vPnC serotype with the lowest GMC, not including serotype 3) in the 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the GMR (20vPnC/lowest 13vPnC) was greater than 0.5 (2-fold criterion).

| | |
|-----------------------------------|---|
| Statistical analysis title | NI of 20vPnC - 13vPnC for 7 additional serotype |
|-----------------------------------|---|

Statistical analysis description:

Serotype 22F: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC - lowest 13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution).

| | |
|---|---------------------------------|
| Comparison groups | 20vPnC v 13vPnC |
| Number of subjects included in analysis | 1500 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[51] |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 5.01 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 4.54 |
| upper limit | 5.52 |

Notes:

[51] - For the additional 7 serotypes, the compared results were from serotype 5 (13vPnC serotype with the lowest GMC, not including serotype 3) in the 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the GMR (20vPnC/lowest 13vPnC) was greater than 0.5 (2-fold criterion).

| | |
|-----------------------------------|---|
| Statistical analysis title | NI of 20vPnC - 13vPnC for 7 additional serotype |
|-----------------------------------|---|

Statistical analysis description:

Serotype 33F: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC - lowest 13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution).

| | |
|---|---------------------------------|
| Comparison groups | 20vPnC v 13vPnC |
| Number of subjects included in analysis | 1500 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[52] |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 4.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 3.99 |
| upper limit | 4.85 |

Notes:

[52] - For the additional 7 serotypes, the compared results were from serotype 5 (13vPnC serotype with the lowest GMC, not including serotype 3) in the 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the GMR (20vPnC/lowest 13vPnC) was greater than 0.5 (2-fold criterion).

Primary: Percentage of Subjects With Prespecified Antibody Levels to Specific Concomitant Vaccine Antigens 1 month After Dose 3

| | |
|-----------------|--|
| End point title | Percentage of Subjects With Prespecified Antibody Levels to Specific Concomitant Vaccine Antigens 1 month After Dose 3 |
|-----------------|--|

End point description:

Concentration of antibody to diphtheria toxoid (predefined level ≥ 0.1 IU/mL), tetanus toxoid (predefined level ≥ 0.1 IU/mL), IgG antibodies to pertussis antigens (pertussis toxin, filamentous hemagglutinin and

pertactin, each with the predefined level as the 5th percentile observed in the 13vPnC group), hepatitis B antibody (in milli-international units per mL [mIU/mL]) (predefined level ≥ 10 mIU/mL), neutralizing antibody (NA) titers to poliovirus types 1, 2, and 3 (predefined level NA titer $\geq 1:8$), Haemophilus influenzae type b (Hib) (≥ 0.15 $\mu\text{g/mL}$) were determined on subsets of sera collected at the immunogenicity time point 1 month after Dose 3. The antibody levels were measured by a validated multiplex Luminex immunoassay. The concomitant immune responses were measured on random subsets. Here, 'Number of Subjects Analysed' = number of participants with valid assay results for the specified antigen at 1 month after Dose 3.

| | |
|----------------------|---------|
| End point type | Primary |
| End point timeframe: | |
| 1 month after Dose 3 | |

| End point values | 20vPnC | 13vPnC | | |
|--|-----------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 370 | 363 | | |
| Units: percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Diphtheria (n=370, 363) | 93.5 (90.5 to 95.8) | 97.8 (95.7 to 99.0) | | |
| Tetanus (n=370, 363) | 99.7 (98.5 to 100.0) | 99.4 (98.0 to 99.9) | | |
| Pertussis (PT) (n=370, 363) | 94.9 (92.1 to 96.9) | 95.0 (92.3 to 97.0) | | |
| Pertussis (FHA) (n=370, 363) | 95.7 (93.1 to 97.5) | 95.0 (92.3 to 97.0) | | |
| Pertussis (PRN) (n=370, 363) | 93.8 (90.8 to 96.0) | 95.0 (92.3 to 97.0) | | |
| hepatitis B surface antigen (HBsAg) (n=118, 127) | 100.0 (96.9 to 100.0) | 100.0 (97.1 to 100.0) | | |
| Poliovirus (Type 1) (n=111, 117) | 100.0 (96.7 to 100.0) | 100 (96.9 to 100.0) | | |
| Poliovirus (Type 2) (n=115, 120) | 100.0 (96.8 to 100.0) | 99.2 (95.4 to 100.0) | | |
| Poliovirus (Type 3) (n=115, 120) | 100.0 (96.8 to 100.0) | 100.0 (97.0 to 100.0) | | |
| Hib ≥ 0.15 $\mu\text{g/mL}$ (n=124, 125) | 100.0 (97.1 to 100.0) | 100.0 (97.1 to 100.0) | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | NI of 20vPnC-13vPnC for concomitant vaccine |
| Statistical analysis description: | |
| Diphtheria: 2-Sided CI was calculated using the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage. | |
| Comparison groups | 20vPnC v 13vPnC |
| Number of subjects included in analysis | 733 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[53] |
| Parameter estimate | Percentage Difference |
| Point estimate | -4.3 |

| Confidence interval | |
|---------------------|---------|
| level | 95 % |
| sides | 2-sided |
| lower limit | -7.5 |
| upper limit | -1.4 |

Notes:

[53] - Noninferiority was declared if the lower bound of the 2-sided 95% CI for the percentage differences (20vPnC - 13vPnC) was greater than -10%.

| Statistical analysis title | NI of 20vPnC-13vPnC for concomitant vaccine |
|----------------------------|---|
|----------------------------|---|

Statistical analysis description:

Tetanus: 2-Sided CI was calculated using the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage.

| | |
|---|---------------------------------|
| Comparison groups | 20vPnC v 13vPnC |
| Number of subjects included in analysis | 733 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[54] |
| Parameter estimate | Percentage Difference |
| Point estimate | 0.3 |

| Confidence interval | |
|---------------------|---------|
| level | 95 % |
| sides | 2-sided |
| lower limit | -1 |
| upper limit | 1.7 |

Notes:

[54] - Noninferiority was declared if the lower bound of the 2-sided 95% CI for the percentage differences (20vPnC - 13vPnC) was greater than -10%.

| Statistical analysis title | NI of 20vPnC-13vPnC for concomitant vaccine |
|----------------------------|---|
|----------------------------|---|

Statistical analysis description:

Pertussis (PT): 2-Sided CI was calculated using the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage.

| | |
|---|---------------------------------|
| Comparison groups | 20vPnC v 13vPnC |
| Number of subjects included in analysis | 733 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[55] |
| Parameter estimate | Percentage Difference |
| Point estimate | -0.2 |

| Confidence interval | |
|---------------------|---------|
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.5 |
| upper limit | 3.1 |

Notes:

[55] - Noninferiority was declared if the lower bound of the 2-sided 95% CI for the percentage differences (20vPnC - 13vPnC) was greater than -10%.

| Statistical analysis title | NI of 20vPnC-13vPnC for concomitant vaccine |
|----------------------------|---|
|----------------------------|---|

Statistical analysis description:

Pertussis (FHA): 2-Sided CI was calculated using the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage.

| | |
|-------------------|-----------------|
| Comparison groups | 20vPnC v 13vPnC |
|-------------------|-----------------|

| | |
|---|---------------------------------|
| Number of subjects included in analysis | 733 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[56] |
| Parameter estimate | Percentage Difference |
| Point estimate | 0.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.5 |
| upper limit | 3.9 |

Notes:

[56] - Noninferiority was declared if the lower bound of the 2-sided 95% CI for the percentage differences (20vPnC - 13vPnC) was greater than -10%.

| | |
|-----------------------------------|---|
| Statistical analysis title | NI of 20vPnC-13vPnC for concomitant vaccine |
|-----------------------------------|---|

Statistical analysis description:

Pertussis (PRN): 2-Sided CI was calculated using the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage. 2-Sided CIs are calculated using the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage.

| | |
|---|---------------------------------|
| Comparison groups | 20vPnC v 13vPnC |
| Number of subjects included in analysis | 733 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[57] |
| Parameter estimate | Percentage Difference |
| Point estimate | -1.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -4.7 |
| upper limit | 2.2 |

Notes:

[57] - Noninferiority was declared if the lower bound of the 2-sided 95% CI for the percentage differences (20vPnC - 13vPnC) was greater than -10%.

| | |
|-----------------------------------|---|
| Statistical analysis title | NI of 20vPnC-13vPnC for concomitant vaccine |
|-----------------------------------|---|

Statistical analysis description:

Poliovirus (Type 2): 2-Sided CI was calculated using the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage.

| | |
|---|---------------------------------|
| Comparison groups | 20vPnC v 13vPnC |
| Number of subjects included in analysis | 733 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[58] |
| Parameter estimate | Percentage Difference |
| Point estimate | 0.8 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.4 |
| upper limit | 4.6 |

Notes:

[58] - Noninferiority was declared if the lower bound of the 2-sided 95% CI for the percentage differences (20vPnC - 13vPnC) was greater than -10%.

| | |
|-----------------------------------|---|
| Statistical analysis title | NI of 20vPnC-13vPnC for concomitant vaccine |
|-----------------------------------|---|

Statistical analysis description:

HBsAg: 2-Sided CI was calculated using the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage.

| | |
|---|---------------------------------|
| Comparison groups | 20vPnC v 13vPnC |
| Number of subjects included in analysis | 733 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[59] |
| Parameter estimate | Percentage Difference |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.2 |
| upper limit | 2.9 |

Notes:

[59] - Noninferiority was declared if the lower bound of the 2-sided 95% CI for the percentage differences (20vPnC - 13vPnC) was greater than -10%.

| | |
|-----------------------------------|---|
| Statistical analysis title | NI of 20vPnC-13vPnC for concomitant vaccine |
|-----------------------------------|---|

Statistical analysis description:

Poliovirus (Type 1): 2-Sided CI was calculated using the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage.

| | |
|---|---------------------------------|
| Comparison groups | 20vPnC v 13vPnC |
| Number of subjects included in analysis | 733 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[60] |
| Parameter estimate | Percentage Difference |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.4 |
| upper limit | 3.2 |

Notes:

[60] - Noninferiority was declared if the lower bound of the 2-sided 95% CI for the percentage differences (20vPnC - 13vPnC) was greater than -10%.

| | |
|-----------------------------------|---|
| Statistical analysis title | NI of 20vPnC-13vPnC for concomitant vaccine |
|-----------------------------------|---|

Statistical analysis description:

Poliovirus (Type 3): 2-Sided CI was calculated using the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage.

| | |
|---|---------------------------------|
| Comparison groups | 20vPnC v 13vPnC |
| Number of subjects included in analysis | 733 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[61] |
| Parameter estimate | Percentage Difference |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.2 |
| upper limit | 3.1 |

Notes:

[61] - Noninferiority was declared if the lower bound of the 2-sided 95% CI for the percentage differences (20vPnC - 13vPnC) was greater than -10%.

| | |
|--|---|
| Statistical analysis title | NI of 20vPnC-13vPnC for concomitant vaccine |
| Statistical analysis description: | |
| Hib (≥ 0.15 $\mu\text{g/mL}$): 2-Sided CI were calculated using the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage. | |
| Comparison groups | 20vPnC v 13vPnC |
| Number of subjects included in analysis | 733 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[62] |
| Parameter estimate | Percentage Difference |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3 |
| upper limit | 3 |

Notes:

[62] - Noninferiority was declared if the lower bound of the 2-sided 95% CI for the percentage differences (20vPnC - 13vPnC) was greater than -10%.

Secondary: Serotype-specific IgG GMCs and GMRs at 1 Month After Dose 3

| | |
|--|---|
| End point title | Serotype-specific IgG GMCs and GMRs at 1 Month After Dose 3 |
| End point description: | |
| Pneumococcal IgG antibody against each of the 20 pneumococcal serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F, 8, 10A, 11A, 12F, 15B, 22F and 33F) was measured using direct binding Luminex assay. Results were expressed as IgG concentrations. GMCs and 2-sided CIs were calculated by exponentiating the mean logarithm of the concentrations and the corresponding CIs based on the Student's t distribution. Dose 3 evaluable immunogenicity population: eligible subjects aged 42-98 days on Dose 1, received assigned vaccine, had valid determinate IgG concentration for at least 1 serotype 1 month post Dose 3, had blood collection within 27-56 days post Dose 3, had not received prohibited vaccines before the blood draw at 1 month post Dose 3, had no major protocol deviations. Here, 'Number of Subjects Analysed' = number of participants with valid IgG concentrations for the specified serotype reported at 1 month after Dose 3. | |
| End point type | Secondary |
| End point timeframe: | |
| 1 month after Dose 3 | |

| End point values | 20vPnC | 13vPnC | | |
|--|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 833 | 803 | | |
| Units: $\mu\text{g/mL}$ | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Serotype 1 (n=833, 802) | 0.74 (0.70 to 0.79) | 1.14 (1.06 to 1.22) | | |
| Serotype 3 (n=833, 802) | 0.36 (0.33 to 0.38) | 0.51 (0.48 to 0.55) | | |
| Serotype 4 (n=833, 802) | 0.75 (0.70 to 0.81) | 1.08 (1.00 to 1.17) | | |
| Serotype 5 (n=833, 802) | 0.66 (0.61 to 0.71) | 0.96 (0.88 to 1.04) | | |

| | | | | |
|---------------------------|---------------------|---------------------|--|--|
| Serotype 6A (n=833, 802) | 1.95 (1.81 to 2.10) | 2.69 (2.48 to 2.92) | | |
| Serotype 6B (n=831, 801) | 0.61 (0.55 to 0.68) | 1.02 (0.91 to 1.14) | | |
| Serotype 7F (n=833, 802) | 1.71 (1.62 to 1.81) | 2.29 (2.16 to 2.43) | | |
| Serotype 9V (n=833, 802) | 0.87 (0.81 to 0.93) | 1.21 (1.12 to 1.30) | | |
| Serotype 14 (n=832, 802) | 2.16 (2.01 to 2.33) | 2.72 (2.51 to 2.95) | | |
| Serotype 18C (n=833, 802) | 1.31 (1.23 to 1.39) | 1.71 (1.59 to 1.84) | | |
| Serotype 19A (n=833, 802) | 0.72 (0.67 to 0.76) | 0.91 (0.85 to 0.97) | | |
| Serotype 19F (n=833, 802) | 1.59 (1.50 to 1.67) | 2.00 (1.88 to 2.12) | | |
| Serotype 23F (n=833, 802) | 0.82 (0.75 to 0.90) | 1.25 (1.14 to 1.37) | | |
| Serotype 8 (n=833, 794) | 1.80 (1.70 to 1.91) | 0.02 (0.02 to 0.02) | | |
| Serotype 10A (n=833, 803) | 1.21 (1.09 to 1.33) | 0.01 (0.01 to 0.01) | | |
| Serotype 11A (n=833, 803) | 1.39 (1.30 to 1.48) | 0.02 (0.01 to 0.02) | | |
| Serotype 12F (n=833, 803) | 0.55 (0.50 to 0.60) | 0.01 (0.01 to 0.01) | | |
| Serotype 15B (n=833, 803) | 4.40 (4.11 to 4.71) | 0.03 (0.02 to 0.03) | | |
| Serotype 22F (n=833, 803) | 3.71 (3.45 to 3.99) | 0.01 (0.00 to 0.01) | | |
| Serotype 33F (n=833, 802) | 1.49 (1.36 to 1.64) | 0.02 (0.01 to 0.02) | | |

Statistical analyses

| Statistical analysis title | NI of 20vPnC-13vPnC for 13 matched serotype |
|--|---|
| Statistical analysis description: | |
| Serotype 1: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC-13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution). | |
| Comparison groups | 20vPnC v 13vPnC |
| Number of subjects included in analysis | 1636 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[63] |
| Parameter estimate | Geometric Mean Ratios |
| Point estimate | 0.65 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.59 |
| upper limit | 0.72 |

Notes:

[63] - Comparison for the 13 matched serotypes for 20vPnC is to the corresponding serotype in 13vPnC group. Noninferiority was declared for if the lower bound of the 2-sided 95% CI for the IgG GMR of 20vPnC to 13vPnC for the serotype is greater than 0.5 (2-fold NI margin).

| | |
|--|---|
| Statistical analysis title | NI of 20vPnC-13vPnC for 13 matched serotype |
| Statistical analysis description: | |
| Serotype 3: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC-13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution). | |
| Comparison groups | 20vPnC v 13vPnC |
| Number of subjects included in analysis | 1636 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[64] |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 0.7 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.64 |
| upper limit | 0.76 |

Notes:

[64] - Comparison for the 13 matched serotypes for 20vPnC is to the corresponding serotype in 13vPnC group. Noninferiority was declared for if the lower bound of the 2-sided 95% CI for the IgG GMR of 20vPnC to 13vPnC for the serotype is greater than 0.5 (2-fold NI margin).

| | |
|--|---|
| Statistical analysis title | NI of 20vPnC-13vPnC for 13 matched serotype |
| Statistical analysis description: | |
| Serotype 4: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC-13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution). | |
| Comparison groups | 20vPnC v 13vPnC |
| Number of subjects included in analysis | 1636 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[65] |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 0.7 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.63 |
| upper limit | 0.78 |

Notes:

[65] - Comparison for the 13 matched serotypes for 20vPnC is to the corresponding serotype in 13vPnC group. Noninferiority was declared for if the lower bound of the 2-sided 95% CI for the IgG GMR of 20vPnC to 13vPnC for the serotype is greater than 0.5 (2-fold NI margin).

| | |
|--|---|
| Statistical analysis title | NI of 20vPnC-13vPnC for 13 matched serotype |
| Statistical analysis description: | |
| Serotype 5: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC-13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution). | |
| Comparison groups | 20vPnC v 13vPnC |
| Number of subjects included in analysis | 1636 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[66] |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 0.69 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.61 |
| upper limit | 0.77 |

Notes:

[66] - Comparison for the 13 matched serotypes for 20vPnC is to the corresponding serotype in 13vPnC group. Noninferiority was declared for if the lower bound of the 2-sided 95% CI for the IgG GMR of 20vPnC to 13vPnC for the serotype is greater than 0.5 (2-fold NI margin).

| | |
|-----------------------------------|---|
| Statistical analysis title | NI of 20vPnC-13vPnC for 13 matched serotype |
|-----------------------------------|---|

Statistical analysis description:

Serotype 6A: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC-13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution).

| | |
|---|---------------------------------|
| Comparison groups | 20vPnC v 13vPnC |
| Number of subjects included in analysis | 1636 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[67] |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 0.72 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.65 |
| upper limit | 0.81 |

Notes:

[67] - Comparison for the 13 matched serotypes for 20vPnC is to the corresponding serotype in 13vPnC group. Noninferiority was declared for if the lower bound of the 2-sided 95% CI for the IgG GMR of 20vPnC to 13vPnC for the serotype is greater than 0.5 (2-fold NI margin).

| | |
|-----------------------------------|---|
| Statistical analysis title | NI of 20vPnC-13vPnC for 13 matched serotype |
|-----------------------------------|---|

Statistical analysis description:

Serotype 6B: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC-13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution).

| | |
|---|---------------------------------|
| Comparison groups | 20vPnC v 13vPnC |
| Number of subjects included in analysis | 1636 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[68] |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 0.6 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.51 |
| upper limit | 0.7 |

Notes:

[68] - Comparison for the 13 matched serotypes for 20vPnC is to the corresponding serotype in 13vPnC group. Noninferiority was declared for if the lower bound of the 2-sided 95% CI for the IgG GMR of 20vPnC to 13vPnC for the serotype is greater than 0.5 (2-fold NI margin).

| | |
|-----------------------------------|---|
| Statistical analysis title | NI of 20vPnC-13vPnC for 13 matched serotype |
|-----------------------------------|---|

Statistical analysis description:

Serotype 7F: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC-13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t

distribution).

| | |
|---|---------------------------------|
| Comparison groups | 20vPnC v 13vPnC |
| Number of subjects included in analysis | 1636 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[69] |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 0.75 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.69 |
| upper limit | 0.81 |

Notes:

[69] - Comparison for the 13 matched serotypes for 20vPnC is to the corresponding serotype in 13vPnC group. Noninferiority was declared for if the lower bound of the 2-sided 95% CI for the IgG GMR of 20vPnC to 13vPnC for the serotype is greater than 0.5 (2-fold NI margin).

| | |
|-----------------------------------|---|
| Statistical analysis title | NI of 20vPnC-13vPnC for 13 matched serotype |
|-----------------------------------|---|

Statistical analysis description:

Serotype 9V: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC-13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution).

| | |
|---|---------------------------------|
| Comparison groups | 20vPnC v 13vPnC |
| Number of subjects included in analysis | 1636 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[70] |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 0.72 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.65 |
| upper limit | 0.8 |

Notes:

[70] - Comparison for the 13 matched serotypes for 20vPnC is to the corresponding serotype in 13vPnC group. Noninferiority was declared for if the lower bound of the 2-sided 95% CI for the IgG GMR of 20vPnC to 13vPnC for the serotype is greater than 0.5 (2-fold NI margin).

| | |
|-----------------------------------|---|
| Statistical analysis title | NI of 20vPnC-13vPnC for 13 matched serotype |
|-----------------------------------|---|

Statistical analysis description:

Serotype 14: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC-13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution).

| | |
|---|---------------------------------|
| Comparison groups | 20vPnC v 13vPnC |
| Number of subjects included in analysis | 1636 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[71] |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 0.79 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.71 |
| upper limit | 0.89 |

Notes:

[71] - Comparison for the 13 matched serotypes for 20vPnC is to the corresponding serotype in 13vPnC group. Noninferiority was declared for if the lower bound of the 2-sided 95% CI for the IgG GMR of 20vPnC to 13vPnC for the serotype is greater than 0.5 (2-fold NI margin).

| | |
|-----------------------------------|---|
| Statistical analysis title | NI of 20vPnC-13vPnC for 13 matched serotype |
|-----------------------------------|---|

Statistical analysis description:

Serotype 18C: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC-13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution).

| | |
|---|---------------------------------|
| Comparison groups | 20vPnC v 13vPnC |
| Number of subjects included in analysis | 1636 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[72] |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 0.77 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.7 |
| upper limit | 0.84 |

Notes:

[72] - Comparison for the 13 matched serotypes for 20vPnC is to the corresponding serotype in 13vPnC group. Noninferiority was declared for if the lower bound of the 2-sided 95% CI for the IgG GMR of 20vPnC to 13vPnC for the serotype is greater than 0.5 (2-fold NI margin).

| | |
|-----------------------------------|---|
| Statistical analysis title | NI of 20vPnC - 13vPnC for 7 additional serotype |
|-----------------------------------|---|

Statistical analysis description:

Serotype 15B: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC - lowest 13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution).

| | |
|---|---------------------------------|
| Comparison groups | 20vPnC v 13vPnC |
| Number of subjects included in analysis | 1636 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[73] |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 4.82 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 4.39 |
| upper limit | 5.3 |

Notes:

[73] - For the additional 7 serotypes, the compared results are from serotype 19A (13vPnC serotype with the lowest GMC, not including serotype 3) in the 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the GMR (20vPnC/lowest 13vPnC) was greater than 0.5 (2-fold criterion).

| | |
|-----------------------------------|---|
| Statistical analysis title | NI of 20vPnC-13vPnC for 13 matched serotype |
|-----------------------------------|---|

Statistical analysis description:

Serotype 19A: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC-13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution).

| | |
|-------------------|-----------------|
| Comparison groups | 20vPnC v 13vPnC |
|-------------------|-----------------|

| | |
|---|---------------------------------|
| Number of subjects included in analysis | 1636 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[74] |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 0.79 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.72 |
| upper limit | 0.86 |

Notes:

[74] - Comparison for the 13 matched serotypes for 20vPnC is to the corresponding serotype in 13vPnC group. Noninferiority was declared for if the lower bound of the 2-sided 95% CI for the IgG GMR of 20vPnC to 13vPnC for the serotype is greater than 0.5 (2-fold NI margin).

| | |
|-----------------------------------|---|
| Statistical analysis title | NI of 20vPnC-13vPnC for 13 matched serotype |
|-----------------------------------|---|

Statistical analysis description:

Serotype 19F: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC-13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution).

| | |
|---|---------------------------------|
| Comparison groups | 20vPnC v 13vPnC |
| Number of subjects included in analysis | 1636 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[75] |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 0.79 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.73 |
| upper limit | 0.86 |

Notes:

[75] - Comparison for the 13 matched serotypes for 20vPnC is to the corresponding serotype in 13vPnC group. Noninferiority was declared for if the lower bound of the 2-sided 95% CI for the IgG GMR of 20vPnC to 13vPnC for the serotype is greater than 0.5 (2-fold NI margin).

| | |
|-----------------------------------|---|
| Statistical analysis title | NI of 20vPnC-13vPnC for 13 matched serotype |
|-----------------------------------|---|

Statistical analysis description:

Serotype 23F: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC-13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution).

| | |
|---|---------------------------------|
| Comparison groups | 20vPnC v 13vPnC |
| Number of subjects included in analysis | 1636 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[76] |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 0.66 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.58 |
| upper limit | 0.75 |

Notes:

[76] - Comparison for the 13 matched serotypes for 20vPnC is to the corresponding serotype in 13vPnC group. Noninferiority was declared for if the lower bound of the 2-sided 95% CI for the IgG GMR of 20vPnC to 13vPnC for the serotype is greater than 0.5 (2-fold NI margin).

| | |
|-----------------------------------|---|
| Statistical analysis title | NI of 20vPnC - 13vPnC for 7 additional serotype |
|-----------------------------------|---|

Statistical analysis description:

Serotype 8: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC - lowest 13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution).

| | |
|---|---------------------------------|
| Comparison groups | 20vPnC v 13vPnC |
| Number of subjects included in analysis | 1636 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[77] |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 1.98 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.81 |
| upper limit | 2.16 |

Notes:

[77] - For the additional 7 serotypes, the compared results are from serotype 19A (13vPnC serotype with the lowest GMC, not including serotype 3) in the 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the GMR (20vPnC/lowest 13vPnC) was greater than 0.5 (2-fold criterion).

| | |
|-----------------------------------|---|
| Statistical analysis title | NI of 20vPnC - 13vPnC for 7 additional serotype |
|-----------------------------------|---|

Statistical analysis description:

Serotype 10A: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC - lowest 13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution).

| | |
|---|---------------------------------|
| Comparison groups | 20vPnC v 13vPnC |
| Number of subjects included in analysis | 1636 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[78] |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 1.32 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.18 |
| upper limit | 1.49 |

Notes:

[78] - For the additional 7 serotypes, the compared results are from serotype 19A (13vPnC serotype with the lowest GMC, not including serotype 3) in the 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the GMR (20vPnC/lowest 13vPnC) was greater than 0.5 (2-fold criterion).

| | |
|-----------------------------------|---|
| Statistical analysis title | NI of 20vPnC - 13vPnC for 7 additional serotype |
|-----------------------------------|---|

Statistical analysis description:

Serotype 11A: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC - lowest 13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution).

| | |
|-------------------|-----------------|
| Comparison groups | 20vPnC v 13vPnC |
|-------------------|-----------------|

| | |
|---|---------------------------------|
| Number of subjects included in analysis | 1636 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[79] |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 1.52 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.39 |
| upper limit | 1.67 |

Notes:

[79] - For the additional 7 serotypes, the compared results are from serotype 19A (13vPnC serotype with the lowest GMC, not including serotype 3) in the 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the GMR (20vPnC/lowest 13vPnC) was greater than 0.5 (2-fold criterion).

| | |
|-----------------------------------|---|
| Statistical analysis title | NI of 20vPnC - 13vPnC for 7 additional serotype |
|-----------------------------------|---|

Statistical analysis description:

Serotype 12F: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC - lowest 13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution).

| | |
|---|---------------------------------|
| Comparison groups | 20vPnC v 13vPnC |
| Number of subjects included in analysis | 1636 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[80] |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 0.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.54 |
| upper limit | 0.67 |

Notes:

[80] - For the additional 7 serotypes, the compared results are from serotype 19A (13vPnC serotype with the lowest GMC, not including serotype 3) in the 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the GMR (20vPnC/lowest 13vPnC) was greater than 0.5 (2-fold criterion).

| | |
|-----------------------------------|---|
| Statistical analysis title | NI of 20vPnC - 13vPnC for 7 additional serotype |
|-----------------------------------|---|

Statistical analysis description:

Serotype 22F: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC - lowest 13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution).

| | |
|---|---------------------------------|
| Comparison groups | 20vPnC v 13vPnC |
| Number of subjects included in analysis | 1636 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[81] |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 4.06 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 3.68 |
| upper limit | 4.48 |

Notes:

[81] - For the additional 7 serotypes, the compared results are from serotype 19A (13vPnC serotype with the lowest GMC, not including serotype 3) in the 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the GMR (20vPnC/lowest 13vPnC) was greater than 0.5 (2-fold criterion).

| | |
|-----------------------------------|---|
| Statistical analysis title | NI of 20vPnC - 13vPnC for 7 additional serotype |
|-----------------------------------|---|

Statistical analysis description:

Serotype 33F: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC - lowest 13vPnC) of the logarithms of the IgG concentrations and the corresponding CI (based on the Student's t distribution).

| | |
|---|---------------------------------|
| Comparison groups | 20vPnC v 13vPnC |
| Number of subjects included in analysis | 1636 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[82] |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 1.64 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.46 |
| upper limit | 1.83 |

Notes:

[82] - For the additional 7 serotypes, the compared results are from serotype 19A (13vPnC serotype with the lowest GMC, not including serotype 3) in the 13vPnC group. Noninferiority was declared if the lower bound of the 2-sided 95% CI for the GMR (20vPnC/lowest 13vPnC) was greater than 0.5 (2-fold criterion).

Secondary: Percentage of Subjects With Predefined IgG Concentrations 1 Month After Dose 4

| | |
|-----------------|--|
| End point title | Percentage of Subjects With Predefined IgG Concentrations 1 Month After Dose 4 |
|-----------------|--|

End point description:

Pre-specified levels of serotypes were as follows: for serotype 1, 3, 4, 6A, 7F, 9V, 14, 18C, 19F, 23F, 8, 10A, 11A, 12F, 15B, 22F, 33F: ≥ 0.35 microgram per mL (mcg/mL), for serotype 5: ≥ 0.23 mcg/mL, for serotype 6B: ≥ 0.10 mcg/mL and for serotype 19A: ≥ 0.12 mcg/mL. "Numbers of Subjects Analyzed" were the denominators and numbers of participants with an IgG concentration \geq the predefined level for the given serotype were the numerator for the percentage calculations. 95% CI was based on the Clopper and Pearson method. Dose 4 evaluable immunogenicity population: eligible subjects aged 42-98 days on Dose 1, received 4 doses to which they were randomized, have at least 1 valid immunogenicity result within 27 to 56 days post Dose 4, and had no other major protocol deviations as determined by the clinician. Here, "Number of Subjects Analyzed" = number of participants with valid IgG concentrations for the specified serotype reported at 1 month after Dose 4.

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

End point timeframe:

1 month after Dose 4

| End point values | 20vPnC | 13vPnC | | |
|----------------------------------|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 755 | 745 | | |
| Units: percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Serotype 1 (n=755, 744) | 94.3 (92.4 to 95.8) | 97.2 (95.7 to 98.2) | | |

| | | | | |
|---------------------------|----------------------|----------------------|--|--|
| Serotype 3 (n=755, 745) | 73.6 (70.3 to 76.8) | 85.8 (83.1 to 88.2) | | |
| Serotype 4 (n=754, 745) | 98.9 (97.9 to 99.5) | 99.1 (98.1 to 99.6) | | |
| Serotype 5 (n=755, 745) | 97.9 (96.6 to 98.8) | 97.7 (96.4 to 98.7) | | |
| Serotype 6A (n=755, 745) | 99.5 (98.6 to 99.9) | 99.7 (99.0 to 100.0) | | |
| Serotype 6B (n=753, 744) | 99.1 (98.1 to 99.6) | 99.5 (98.6 to 99.9) | | |
| Serotype 7F (n=755, 745) | 99.5 (98.6 to 99.9) | 99.9 (99.3 to 100.0) | | |
| Serotype 9V (n=755, 744) | 98.5 (97.4 to 99.3) | 98.9 (97.9 to 99.5) | | |
| Serotype 14 (n=755, 745) | 98.9 (97.9 to 99.5) | 99.5 (98.6 to 99.9) | | |
| Serotype 18C (n=755, 745) | 98.9 (97.9 to 99.5) | 99.5 (98.6 to 99.9) | | |
| Serotype 19A (n=754, 745) | 99.9 (99.3 to 100.0) | 99.7 (99.0 to 100.0) | | |
| Serotype 19F (n=755, 745) | 98.8 (97.7 to 99.5) | 98.9 (97.9 to 99.5) | | |
| Serotype 23F (n=755, 745) | 97.2 (95.8 to 98.3) | 98.1 (96.9 to 99.0) | | |
| Serotype 8 (n=755, 720) | 99.5 (98.6 to 99.9) | 4.7 (3.3 to 6.5) | | |
| Serotype 10A (n=755, 744) | 97.7 (96.4 to 98.7) | 2.0 (1.1 to 3.3) | | |
| Serotype 11A (n=755, 745) | 98.8 (97.7 to 99.5) | 4.2 (2.8 to 5.9) | | |
| Serotype 12F (n=755, 745) | 95.2 (93.5 to 96.6) | 0.3 (0.0 to 1.0) | | |
| Serotype 15B (n=755, 745) | 99.7 (99.0 to 100.0) | 4.6 (3.2 to 6.3) | | |
| Serotype 22F (n=755, 745) | 99.6 (98.8 to 99.9) | 1.5 (0.7 to 2.6) | | |
| Serotype 33F (n=755, 745) | 99.5 (98.6 to 99.9) | 1.7 (0.9 to 3.0) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Serotype-specific opsonophagocytic activity (OPA) Geometric Mean Titers (GMTs) at 1 Month After Dose 3

| | |
|-----------------|--|
| End point title | Serotype-specific opsonophagocytic activity (OPA) Geometric Mean Titers (GMTs) at 1 Month After Dose 3 |
|-----------------|--|

End point description:

OPA titers for the 20 pneumococcal serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F, 8, 10A, 11A, 12F, 15B, 22F, and 33F) were determined in randomized subsets of participants at 1 month after Dose 3. Results were expressed as OPA titers. GMTs and 2-sided CIs were calculated by exponentiating the mean logarithm of the concentrations and the corresponding CIs based on the Student's t distribution. Dose 3 evaluable immunogenicity population: eligible subjects aged 42-98 days on Dose 1, received the first 3 doses to which they were randomized, have at least 1 valid immunogenicity result within 27 to 56 days after Dose 3, and had no other major protocol deviations as determined by the clinician. Here, "Number of Subjects Analyzed" = number of participants with valid OPA titers for the specified serotype reported at 1 month after Dose 3.

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

End point timeframe:

1 month after Dose 3

| End point values | 20vPnC | 13vPnC | | |
|--|----------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 103 | 113 | | |
| Units: Titers | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Serotype 1 (n=103, 98) | 26 (21 to 33) | 34 (27 to 42) | | |
| Serotype 3 (n=105, 97) | 51 (43 to 61) | 63 (53 to 76) | | |
| Serotype 4 (n=97, 90) | 339 (252 to 455) | 280 (207 to 378) | | |
| Serotype 5 (n=103, 98) | 32 (27 to 39) | 39 (32 to 47) | | |
| Serotype 6A (n=104, 96) | 910 (763 to 1084) | 936 (757 to 1156) | | |
| Serotype 6B (n=99, 91) | 318 (242 to 419) | 516 (409 to 651) | | |
| Serotype 7F (n=91, 87) | 1222 (1020 to 1465) | 1149 (926 to 1424) | | |
| Serotype 9V (n=94, 87) | 661 (482 to 906) | 594 (421 to 838) | | |
| Serotype 14 (n=103, 97) | 415 (323 to 535) | 420 (330 to 535) | | |
| Serotype 18C (n=95, 87) | 1153 (910 to 1460) | 996 (754 to 1317) | | |
| Serotype 19A (n=93, 84) | 108 (78 to 149) | 109 (79 to 151) | | |
| Serotype 19F (n=102, 97) | 84 (67 to 105) | 116 (90 to 149) | | |
| Serotype 23F (n=96, 86) | 255 (186 to 350) | 295 (215 to 406) | | |
| Serotype 8 (n=100, 112) | 665 (503 to 880) | 18 (17 to 20) | | |
| Serotype 10A (n=101, 109) | 2558 (1869 to 3501) | 37 (33 to 42) | | |
| Serotype 11A (n=100, 108) | 289 (212 to 395) | 50 (46 to 55) | | |
| Serotype 12F (n=92, 110) | 7677 (5952 to 9901) | 28 (24 to 33) | | |
| Serotype 15B (n=97, 110) | 1560 (1090 to 2233) | 18 (16 to 22) | | |
| Serotype 22F (n=97, 113) | 6797 (5170 to 8936) | 9 (9 to 9) | | |
| Serotype 33F (n=85, 111) | 7388 (4803 to 11365) | 198 (177 to 220) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Serotype-specific OPA GMTs at 1 Month After Dose 4

| | |
|--|--|
| End point title | Serotype-specific OPA GMTs at 1 Month After Dose 4 |
| End point description: | |
| <p>OPA titers for the 20 pneumococcal serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F, 8, 10A, 11A, 12F, 15B, 22F, and 33F) were determined in randomized subsets of participants at 1 month after Dose 4. Results were expressed as OPA titers. GMTs and 2-sided CIs were calculated by exponentiating the mean logarithm of the concentrations and the corresponding CIs based on the Student's t distribution. Dose 4 evaluable immunogenicity population: eligible subjects aged 42-98 days on Dose 1, received all 4 doses as randomized, have at least 1 valid immunogenicity result within 27 to 56 days after Dose 4, and had no other major protocol deviations as determined by the clinician. Here, "Number of Subjects Analyzed" = number of participants with valid OPA titers for the specified serotype reported at 1 month after Dose 4.</p> | |
| End point type | Secondary |
| End point timeframe: | |
| 1 month after Dose 4 | |

| End point values | 20vPnC | 13vPnC | | |
|--|-----------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 99 | 103 | | |
| Units: Titers | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Serotype 1 (n=94, 91) | 36 (27 to 48) | 66 (50 to 87) | | |
| Serotype 3 (n=92, 88) | 62 (49 to 78) | 102 (86 to 120) | | |
| Serotype 4 (n=85, 82) | 621 (435 to 887) | 961 (714 to 1294) | | |
| Serotype 5 (n=94, 91) | 55 (45 to 67) | 69 (54 to 87) | | |
| Serotype 6A (n=93, 91) | 1384 (1092 to 1753) | 1767 (1329 to 2348) | | |
| Serotype 6B (n=92, 88) | 666 (489 to 906) | 1211 (861 to 1703) | | |
| Serotype 7F (n=84, 81) | 2022 (1673 to 2444) | 2099 (1741 to 2531) | | |
| Serotype 9V (n=85, 79) | 2609 (1913 to 3558) | 3210 (2500 to 4123) | | |
| Serotype 14 (n=92, 91) | 667 (523 to 850) | 593 (462 to 761) | | |
| Serotype 18C (n=84, 83) | 1973 (1472 to 2643) | 2425 (1914 to 3072) | | |
| Serotype 19A (n=85, 78) | 844 (622 to 1145) | 1357 (1007 to 1829) | | |
| Serotype 19F (n=93, 91) | 246 (179 to 337) | 373 (272 to 513) | | |
| Serotype 23F (n=84, 77) | 827 (554 to 1235) | 1532 (1118 to 2100) | | |
| Serotype 8 (n=89, 97) | 1228 (901 to 1673) | 26 (21 to 31) | | |
| Serotype 10A (n=99, 102) | 3674 (2746 to 4916) | 57 (44 to 74) | | |
| Serotype 11A (n=90, 89) | 2728 (1975 to 3768) | 69 (53 to 89) | | |
| Serotype 12F (n=86, 103) | 9320 (7037 to 12343) | 31 (26 to 37) | | |
| Serotype 15B (n=92, 100) | 3035 (2138 to 4308) | 23 (17 to 30) | | |
| Serotype 22F (n=86, 101) | 11077 (7956 to 15422) | 15 (11 to 20) | | |

| | | | | |
|-------------------------|------------------------|------------------|--|--|
| Serotype 33F (n=80, 97) | 19216 (13193 to 27990) | 363 (292 to 451) | | |
|-------------------------|------------------------|------------------|--|--|

Statistical analyses

No statistical analyses for this end point

Secondary: Serotype-specific IgG Geometric Mean Fold Rise (GMFRs) From 1 Month After Dose 3 to Before Dose 4

| | |
|------------------------|---|
| End point title | Serotype-specific IgG Geometric Mean Fold Rise (GMFRs) From 1 Month After Dose 3 to Before Dose 4 |
| End point description: | GMFR of pneumococcal 20vPnC serotypes included: 1, 3, 4, 5, 6A, 6B, 7F, 8, 9V, 10A, 11A, 12F, 14, 15B, 18C, 19A, 19F, 22F, 23F and 33F. The GMFR from 1 month after Dose 3 to before Dose 4 were reported from Dose 3 evaluable immunogenicity subjects. Here, "Number of Subjects Analyzed" = subject evaluable for this endpoint and with valid IgG concentrations at both timepoints for the specified serotype. |
| End point type | Secondary |
| End point timeframe: | 1 month after Dose 3 to before Dose 4 |

| End point values | 20vPnC | 13vPnC | | |
|--|------------------|------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 758 | 733 | | |
| Units: Fold rise | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Serotype 1 (n=758, 733) | 0.3 (0.3 to 0.3) | 0.3 (0.2 to 0.3) | | |
| Serotype 3 (n=758, 733) | 0.2 (0.2 to 0.2) | 0.2 (0.2 to 0.2) | | |
| Serotype 4 (n=758, 733) | 0.3 (0.3 to 0.4) | 0.3 (0.3 to 0.3) | | |
| Serotype 5 (n=758, 733) | 0.3 (0.3 to 0.3) | 0.3 (0.3 to 0.3) | | |
| Serotype 6A (n=758, 732) | 0.3 (0.3 to 0.3) | 0.3 (0.3 to 0.3) | | |
| Serotype 6B (n=754, 730) | 0.4 (0.4 to 0.4) | 0.3 (0.3 to 0.3) | | |
| Serotype 7F (n=758, 733) | 0.4 (0.4 to 0.6) | 0.4 (0.3 to 0.4) | | |
| Serotype 9V (n=758, 733) | 0.3 (0.3 to 0.4) | 0.3 (0.3 to 0.3) | | |
| Serotype 14 (n=757, 733) | 0.5 (0.4 to 0.5) | 0.5 (0.4 to 0.5) | | |
| Serotype 18C (n=758, 733) | 0.2 (0.2 to 0.2) | 0.2 (0.2 to 0.2) | | |
| Serotype 19A (n=757, 733) | 0.2 (0.2 to 0.2) | 0.2 (0.2 to 0.2) | | |
| Serotype 19F (n=758, 733) | 0.2 (0.2 to 0.3) | 0.2 (0.2 to 0.2) | | |
| Serotype 23F (n=758, 733) | 0.3 (0.3 to 0.3) | 0.3 (0.2 to 0.3) | | |
| Serotype 8 (n=758, 706) | 0.2 (0.2 to 0.3) | 1.4 (1.3 to 1.5) | | |
| Serotype 10A (n=758, 732) | 0.7 (0.6 to 0.7) | 0.9 (0.9 to 1.0) | | |
| Serotype 11A (n=758, 732) | 0.3 (0.2 to 0.3) | 1.1 (1.0 to 1.2) | | |
| Serotype 12F (n=758, 732) | 0.3 (0.3 to 0.4) | 1.0 (1.0 to 1.1) | | |
| Serotype 15B (n=758, 732) | 0.4 (0.3 to 0.4) | 0.8 (0.7 to 0.8) | | |
| Serotype 22F (n=758, 732) | 0.3 (0.3 to 0.4) | 0.8 (0.7 to 0.9) | | |
| Serotype 33F (n=758, 731) | 0.7 (0.7 to 0.8) | 0.8 (0.7 to 0.8) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Serotype-specific IgG GMFRs From 1 Month Before to 1 month After Dose 4

| | |
|-----------------|---|
| End point title | Serotype-specific IgG GMFRs From 1 Month Before to 1 month After Dose 4 |
|-----------------|---|

End point description:

GMFR of pneumococcal 20vPnC serotypes included: 1, 3, 4, 5, 6A, 6B, 7F, 8, 9V, 10A, 11A, 12F, 14, 15B, 18C, 19A, 19F, 22F, 23F and 33F. The GMFR from 1 month before Dose 4 to 1 month after Dose 4 were reported from Dose 4 evaluable immunogenicity subjects. Here "Number of Subjects Analyzed" = subject evaluable for this endpoint and with valid IgG concentrations at both timepoints for the specified serotype.

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

End point timeframe:

From 1 month before to 1 month after Dose 4

| End point values | 20vPnC | 13vPnC | | |
|--|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 732 | 721 | | |
| Units: Fold rise | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Serotype 1 (n=732, 720) | 7.3 (6.9 to 7.8) | 7.1 (6.7 to 7.6) | | |
| Serotype 3 (n=732, 721) | 8.5 (7.9 to 9.1) | 9.0 (8.4 to 9.6) | | |
| Serotype 4 (n=731, 721) | 15.4 (14.3 to 16.6) | 14.2 (13.1 to 15.3) | | |
| Serotype 6A (n=732, 720) | 15.2 (14.3 to 16.2) | 14.5 (13.5 to 15.5) | | |
| Serotype 6B (n=727, 718) | 18.0 (16.8 to 19.3) | 17.0 (15.8 to 18.2) | | |
| Serotype 7F (n=732, 721) | 6.0 (5.7 to 6.3) | 6.4 (6.0 to 6.8) | | |
| Serotype 9V (n=732, 720) | 11.8 (11.1 to 12.6) | 11.2 (10.5 to 11.9) | | |
| Serotype 14 (n=732, 721) | 5.9 (5.4 to 6.3) | 5.0 (4.6 to 5.3) | | |
| Serotype 5 (n=732, 721) | 8.9 (8.4 to 9.5) | 8.5 (8.0 to 9.0) | | |
| Serotype 18C (n=732, 721) | 11.3 (10.6 to 12.0) | 11.4 (10.7 to 12.1) | | |
| Serotype 19A (n=731, 721) | 25.6 (23.8 to 27.6) | 25.6 (23.6 to 27.7) | | |
| Serotype 19F (n=732, 721) | 13.1 (12.2 to 14.1) | 12.5 (11.6 to 13.5) | | |
| Serotype 23F (n=732, 721) | 18.1 (16.8 to 19.5) | 19.2 (17.9 to 20.6) | | |
| Serotype 8 (n=732, 692) | 9.1 (8.5 to 9.8) | 1.3 (1.2 to 1.4) | | |
| Serotype 10A (n=732, 718) | 8.1 (7.6 to 8.7) | 1.1 (1.0 to 1.1) | | |

| | | | | |
|---------------------------|--------------------|------------------|--|--|
| Serotype 11A (n=732, 719) | 9.8 (9.1 to 10.6) | 1.1 (1.0 to 1.2) | | |
| Serotype 12F (n=732, 719) | 10.0 (9.4 to 10.6) | 1.0 (1.0 to 1.1) | | |
| Serotype 15B (n=732, 719) | 8.1 (7.5 to 8.7) | 1.2 (1.2 to 1.3) | | |
| Serotype 22F (n=732, 719) | 8.4 (7.9 to 9.1) | 1.2 (1.1 to 1.3) | | |
| Serotype 33F (n=732, 719) | 8.8 (8.2 to 9.4) | 1.1 (1.0 to 1.1) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Serotype-specific IgG GMFRs From 1 Month After Dose 3 to 1 Month After Dose 4

| | |
|------------------------|---|
| End point title | Serotype-specific IgG GMFRs From 1 Month After Dose 3 to 1 Month After Dose 4 |
| End point description: | GMFR of pneumococcal 20vPnC serotypes included: 1, 3, 4, 5, 6A, 6B, 7F, 8, 9V, 10A, 11A, 12F, 14, 15B, 18C, 19A, 19F, 22F, 23F and 33F. The GMFR from 1 month after Dose 3 to 1 month after Dose 4 were reported from subjects in both Dose 3 and Dose 4 evaluable immunogenicity populations. Here, "Number of Subjects Analyzed" = subject evaluable for this endpoint and with valid IgG concentrations at both timepoints for the specified serotype. |
| End point type | Secondary |
| End point timeframe: | from 1 month after Dose 3 to 1 month after Dose 4 |

| End point values | 20vPnC | 13vPnC | | |
|--|------------------|------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 704 | 687 | | |
| Units: Fold rise | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Serotype 1 (n=704, 685) | 2.0 (1.9 to 2.1) | 1.8 (1.7 to 1.9) | | |
| Serotype 3 (n=704, 686) | 1.6 (1.5 to 1.7) | 1.7 (1.6 to 1.8) | | |
| Serotype 4 (n=703, 686) | 5.1 (4.8 to 5.5) | 4.4 (4.1 to 4.8) | | |
| Serotype 5 (n=704, 686) | 2.9 (2.7 to 3.1) | 2.6 (2.4 to 2.8) | | |
| Serotype 6A (n=704, 686) | 4.7 (4.4 to 5.0) | 4.3 (4.0 to 4.6) | | |
| Serotype 6B (n=700, 685) | 6.8 (6.2 to 7.4) | 5.5 (5.0 to 6.0) | | |
| Serotype 7F (n=704, 686) | 2.3 (2.2 to 2.4) | 2.2 (2.1 to 2.3) | | |
| Serotype 9V (n=704, 685) | 4.0 (3.7 to 4.3) | 3.4 (3.2 to 3.7) | | |
| Serotype 14 (n=703, 686) | 2.6 (2.4 to 2.9) | 2.2 (2.0 to 2.5) | | |
| Serotype 18C (n=704, 686) | 2.7 (2.5 to 2.8) | 2.6 (2.5 to 2.8) | | |
| Serotype 19A (n=703, 686) | 4.9 (4.6 to 5.2) | 4.6 (4.2 to 4.9) | | |
| Serotype 19F (n=704, 686) | 3.2 (3.0 to 3.4) | 2.9 (2.7 to 3.1) | | |
| Serotype 23F (n=704, 686) | 4.9 (4.5 to 5.3) | 4.9 (4.5 to 5.3) | | |
| Serotype 8 (n=704, 659) | 2.2 (2.0 to 2.3) | 1.8 (1.6 to 2.0) | | |
| Serotype 10A (n=704, 686) | 5.3 (4.9 to 5.8) | 1.0 (0.9 to 1.1) | | |
| Serotype 11A (n=704, 687) | 2.6 (2.4 to 2.8) | 1.1 (1.0 to 1.3) | | |
| Serotype 12F (n=704, 687) | 3.3 (3.1 to 3.6) | 1.0 (1.0 to 1.1) | | |

| | | | | |
|---------------------------|------------------|------------------|--|--|
| Serotype 15B (n=704, 687) | 2.8 (2.6 to 3.0) | 1.0 (0.9 to 1.1) | | |
| Serotype 22F (n=704, 687) | 2.9 (2.7 to 3.1) | 1.0 (0.9 to 1.1) | | |
| Serotype 33F (n=704, 686) | 6.4 (5.9 to 7.0) | 0.8 (0.8 to 0.9) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Alternative Prespecified Hib Antibody Level 1 Month After Dose 3

| | |
|-----------------|--|
| End point title | Percentage of Subjects With Alternative Prespecified Hib Antibody Level 1 Month After Dose 3 |
|-----------------|--|

End point description:

Antibody concentration to the Hib vaccine antigens were determined on sera collected from randomly selected subsets of participants with sufficient sera volumes. Percentage of subjects with alternative prespecified Hib antibody (≥ 1.0 $\mu\text{g/mL}$) were reported from Dose 3 evaluable immunogenicity subjects. Subjects analyzed were restricted to those participants who received the appropriate concomitant vaccines with the first 3 doses. Here, "Number of Subjects Analyzed" = number of participants with valid Hib antibody level for the specified antigen.

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

End point timeframe:

1 month after Dose 3

| End point values | 20vPnC | 13vPnC | | |
|----------------------------------|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 124 | 125 | | |
| Units: percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| ≥ 1.0 $\mu\text{g/mL}$ | 75.0 (66.4 to 82.3) | 72.0 (63.3 to 79.7) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Ratios (GMRs) of Prespecified Antibody Levels to Specific Concomitant Vaccine Antigens 1 month after Dose 4

| | |
|-----------------|--|
| End point title | Geometric Mean Ratios (GMRs) of Prespecified Antibody Levels to Specific Concomitant Vaccine Antigens 1 month after Dose 4 |
|-----------------|--|

End point description:

Antibody concentrations to each concomitant vaccine antigen (measles, mumps, rubella, and varicella) were determined on sera collected 1 month after Dose 4 from a randomly selected subset of participants with sufficient sera volumes. GMs and 2-sided CIs were calculated by exponentiating the mean logarithm of the concentrations and the corresponding CIs based on the Student's t distribution and were reported from Dose 4 evaluable immunogenicity subjects. Dose 4 evaluable immunogenicity population restricted to those who received the corresponding concomitant vaccine with the specified concomitant vaccine antigen. Here, "Number of Subjects Analyzed" = number of participants with valid antibody concentrations for the specified antigen reported at 1 month after Dose 4.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| 1 month after Dose 4 | |

| End point values | 20vPnC | 13vPnC | | |
|--|---------------------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 234 | 232 | | |
| Units: see the table below | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Measles (AU/mL) (n=234, 232) | 277.74 (243.88 to 316.30) | 215.41 (184.61 to 251.35) | | |
| Mumps (AU/mL) (n=234, 232) | 36.96 (30.82 to 44.33) | 34.19 (28.94 to 40.39) | | |
| Rubella (IU/mL) (n=234, 232) | 49.63 (43.88 to 56.13) | 40.44 (35.19 to 46.48) | | |
| Varicella (mIU/mL) (n=231, 229) | 233.05 (207.25 to 262.06) | 234.78 (208.84 to 263.94) | | |

Statistical analyses

| | |
|-----------------------------------|---|
| Statistical analysis title | NI of 20vPnC-13vPnC for vaccine antigen |
|-----------------------------------|---|

Statistical analysis description:

Measles: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC - 13vPnC) of the logarithms of the concentrations and the corresponding CI (based on the Student's t distribution).

| | |
|---|---------------------------------|
| Comparison groups | 20vPnC v 13vPnC |
| Number of subjects included in analysis | 466 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[83] |
| Parameter estimate | Geometric Mean Ratios |
| Point estimate | 1.29 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.05 |
| upper limit | 1.58 |

Notes:

[83] - Noninferiority was declared if the lower bound of the 2-sided 95% CI for the GMR of 20vPnC group to 13vPnC group is greater than 0.5 (2-fold NI margin).

| | |
|-----------------------------------|---|
| Statistical analysis title | NI of 20vPnC-13vPnC for vaccine antigen |
|-----------------------------------|---|

Statistical analysis description:

Varicella: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC - 13vPnC) of the logarithms of the concentrations and the corresponding CI (based on the Student's t distribution).

| | |
|-------------------|-----------------|
| Comparison groups | 20vPnC v 13vPnC |
|-------------------|-----------------|

| | |
|---|---------------------------------|
| Number of subjects included in analysis | 466 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[84] |
| Parameter estimate | Geometric Mean Ratios |
| Point estimate | 0.99 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.84 |
| upper limit | 1.17 |

Notes:

[84] - Noninferiority was declared if the lower bound of the 2-sided 95% CI for the GMR of 20vPnC group to 13vPnC group is greater than 0.5 (2-fold NI margin).

| | |
|-----------------------------------|---|
| Statistical analysis title | NI of 20vPnC-13vPnC for vaccine antigen |
|-----------------------------------|---|

Statistical analysis description:

Rubella: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC - 13vPnC) of the logarithms of the concentrations and the corresponding CI (based on the Student's t distribution).

| | |
|---|---------------------------------|
| Comparison groups | 20vPnC v 13vPnC |
| Number of subjects included in analysis | 466 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[85] |
| Parameter estimate | Geometric Mean Ratios |
| Point estimate | 1.23 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.02 |
| upper limit | 1.48 |

Notes:

[85] - Noninferiority was declared if the lower bound of the 2-sided 95% CI for the GMR of 20vPnC group to 13vPnC group is greater than 0.5 (2-fold NI margin).

| | |
|-----------------------------------|---|
| Statistical analysis title | NI of 20vPnC-13vPnC for vaccine antigen |
|-----------------------------------|---|

Statistical analysis description:

Mumps: GMR and 2-Sided CI were calculated by exponentiating the mean difference (20vPnC - 13vPnC) of the logarithms of the concentrations and the corresponding CI (based on the Student's t distribution).

| | |
|---|---------------------------------|
| Comparison groups | 20vPnC v 13vPnC |
| Number of subjects included in analysis | 466 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[86] |
| Parameter estimate | Geometric Mean Ratios |
| Point estimate | 1.08 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.85 |
| upper limit | 1.38 |

Notes:

[86] - Noninferiority was declared if the lower bound of the 2-sided 95% CI for the GMR of 20vPnC group to 13vPnC group is greater than 0.5 (2-fold NI margin).

Adverse events

Adverse events information

Timeframe for reporting adverse events:

LR and SE [systematic assessment(SA)]:within 7 days after Dose 1, 2, 3, 4; SAEs: from Dose 1 up to 6 months after Dose 4; other AEs [non-systematic assessment (non-SA)]:from Dose 1 up to 1 month after Dose 3 and from Dose 4 up to 1 month after Dose 4

Adverse event reporting additional description:

Same events may appear as both an AE and a SAE. However, what are presented are distinct events. An event may be classified as serious in 1 subject and as non-serious in another subject, or 1 subject may have experienced both a SAE and non-SAE during the study

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 25.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--------|
| Reporting group title | 13vPnC |
|-----------------------|--------|

Reporting group description:

Infants 42 to 98 days of age were enrolled to receive 4 doses of 0.5 millilitre (mL) 13-valent Pneumococcal Conjugate Vaccine (13vPnC) intramuscularly. Dose 1 was given at enrollment and Dose 2 and 3 were given 42 to 63 days from the previous dose. Dose 4 was administered at 365 to 455 days of age.

| | |
|-----------------------|--------|
| Reporting group title | 20vPnC |
|-----------------------|--------|

Reporting group description:

Infants 42 to 98 days of age were enrolled to receive 4 doses of 0.5 millilitre (mL) 20-valent Pneumococcal Conjugate Vaccine (20vPnC) intramuscularly. Dose 1 was given at enrollment and Dose 2 and 3 were given 42 to 63 days from the previous dose. Dose 4 was administered at 365 to 455 days of age.

| Serious adverse events | 13vPnC | 20vPnC | |
|---|------------------|-------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 31 / 987 (3.14%) | 45 / 1001 (4.50%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | | | |
| Injury, poisoning and procedural complications | | | |
| Thermal burn | | | |
| subjects affected / exposed | 1 / 987 (0.10%) | 0 / 1001 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Subdural haematoma | | | |
| subjects affected / exposed | 0 / 987 (0.00%) | 1 / 1001 (0.10%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skull fracture | | | |

| | | | |
|---|-----------------|------------------|--|
| subjects affected / exposed | 0 / 987 (0.00%) | 1 / 1001 (0.10%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fall | | | |
| subjects affected / exposed | 0 / 987 (0.00%) | 1 / 1001 (0.10%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Extradural haematoma | | | |
| subjects affected / exposed | 0 / 987 (0.00%) | 1 / 1001 (0.10%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Accidental poisoning | | | |
| subjects affected / exposed | 1 / 987 (0.10%) | 0 / 1001 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Accidental exposure to product | | | |
| subjects affected / exposed | 0 / 987 (0.00%) | 1 / 1001 (0.10%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| Kawasaki's disease | | | |
| subjects affected / exposed | 0 / 987 (0.00%) | 1 / 1001 (0.10%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Partial seizures | | | |
| subjects affected / exposed | 1 / 987 (0.10%) | 0 / 1001 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypoglycaemic seizure | | | |
| subjects affected / exposed | 1 / 987 (0.10%) | 0 / 1001 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Febrile convulsion | | | |

| | | | |
|---|-----------------|------------------|--|
| subjects affected / exposed | 2 / 987 (0.20%) | 2 / 1001 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Status epilepticus | | | |
| subjects affected / exposed | 1 / 987 (0.10%) | 0 / 1001 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Systemic inflammatory response syndrome | | | |
| subjects affected / exposed | 0 / 987 (0.00%) | 1 / 1001 (0.10%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| Immune thrombocytopenia | | | |
| subjects affected / exposed | 0 / 987 (0.00%) | 1 / 1001 (0.10%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 987 (0.00%) | 1 / 1001 (0.10%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Microcytic anaemia | | | |
| subjects affected / exposed | 1 / 987 (0.10%) | 0 / 1001 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Vomiting | | | |
| subjects affected / exposed | 0 / 987 (0.00%) | 1 / 1001 (0.10%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intussusception | | | |

| | | | |
|--|-----------------|------------------|--|
| subjects affected / exposed | 1 / 987 (0.10%) | 0 / 1001 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute respiratory failure | | | |
| subjects affected / exposed | 1 / 987 (0.10%) | 0 / 1001 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Asthma | | | |
| subjects affected / exposed | 1 / 987 (0.10%) | 0 / 1001 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Bullous impetigo | | | |
| subjects affected / exposed | 0 / 987 (0.00%) | 1 / 1001 (0.10%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchiolitis | | | |
| subjects affected / exposed | 4 / 987 (0.41%) | 4 / 1001 (0.40%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Adenovirus infection | | | |
| subjects affected / exposed | 0 / 987 (0.00%) | 1 / 1001 (0.10%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dengue fever | | | |
| subjects affected / exposed | 0 / 987 (0.00%) | 1 / 1001 (0.10%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| COVID-19 | | | |
| subjects affected / exposed | 1 / 987 (0.10%) | 0 / 1001 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|-----------------|------------------|--|
| Cellulitis | | | |
| subjects affected / exposed | 0 / 987 (0.00%) | 1 / 1001 (0.10%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Coronavirus infection | | | |
| subjects affected / exposed | 0 / 987 (0.00%) | 1 / 1001 (0.10%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Croup infectious | | | |
| subjects affected / exposed | 0 / 987 (0.00%) | 1 / 1001 (0.10%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia necrotising | | | |
| subjects affected / exposed | 1 / 987 (0.10%) | 0 / 1001 (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 | 1 / 987 (0.10%) | 2 / 1001 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metapneumovirus bronchiolitis | | | |
| subjects affected / exposed | 1 / 987 (0.10%) | 0 / 1001 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hand-foot-and-mouth disease | | | |
| subjects affected / exposed | 1 / 987 (0.10%) | 1 / 1001 (0.10%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Groin abscess | | | |
| subjects affected / exposed | 0 / 987 (0.00%) | 1 / 1001 (0.10%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal viral infection | | | |

| | | |
|---|-----------------|------------------|
| subjects affected / exposed | 0 / 987 (0.00%) | 1 / 1001 (0.10%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 |
| Gastroenteritis norovirus | | |
| subjects affected / exposed | 0 / 987 (0.00%) | 1 / 1001 (0.10%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 |
| Gastroenteritis | | |
| subjects affected / exposed | 5 / 987 (0.51%) | 0 / 1001 (0.00%) |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 |
| Escherichia urinary tract infection | | |
| subjects affected / exposed | 2 / 987 (0.20%) | 0 / 1001 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 |
| Pneumonia respiratory syncytial viral | | |
| subjects affected / exposed | 0 / 987 (0.00%) | 1 / 1001 (0.10%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 |
| Respiratory syncytial virus infection | | |
| subjects affected / exposed | 2 / 987 (0.20%) | 5 / 1001 (0.50%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 |
| Respiratory syncytial virus bronchiolitis | | |
| subjects affected / exposed | 3 / 987 (0.30%) | 7 / 1001 (0.70%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 7 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 |
| Pyelonephritis acute | | |
| subjects affected / exposed | 0 / 987 (0.00%) | 1 / 1001 (0.10%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 |
| Respiratory tract infection viral | | |

| | | | |
|---|-----------------|------------------|--|
| subjects affected / exposed | 1 / 987 (0.10%) | 0 / 1001 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 987 (0.00%) | 1 / 1001 (0.10%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract infection pseudomonal | | | |
| subjects affected / exposed | 1 / 987 (0.10%) | 0 / 1001 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Viral infection | | | |
| subjects affected / exposed | 1 / 987 (0.10%) | 1 / 1001 (0.10%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Otitis media acute | | | |
| subjects affected / exposed | 0 / 987 (0.00%) | 1 / 1001 (0.10%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Failure to thrive | | | |
| subjects affected / exposed | 1 / 987 (0.10%) | 2 / 1001 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dehydration | | | |
| subjects affected / exposed | 1 / 987 (0.10%) | 2 / 1001 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | 13vPnC | 20vPnC | |
|---|--------------------|---------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 939 / 987 (95.14%) | 966 / 1001 (96.50%) | |
| Nervous system disorders | | | |
| Hypersomnia (INCREASED SLEEP) | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 798 / 987 (80.85%) | 823 / 1001 (82.22%) | |
| occurrences (all) | 2268 | 2309 | |
| General disorders and administration site conditions | | | |
| Pyrexia (FEVER) | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 314 / 987 (31.81%) | 322 / 1001 (32.17%) | |
| occurrences (all) | 504 | 550 | |
| Injection site swelling (SWELLING) | | | |
| subjects affected / exposed | 359 / 987 (36.37%) | 353 / 1001 (35.26%) | |
| occurrences (all) | 707 | 635 | |
| Injection site pain (PAIN) | | | |
| subjects affected / exposed | 663 / 987 (67.17%) | 689 / 1001 (68.83%) | |
| occurrences (all) | 1543 | 1634 | |
| Injection site erythema (REDNESS) | | | |
| subjects affected / exposed | 492 / 987 (49.85%) | 498 / 1001 (49.75%) | |
| occurrences (all) | 986 | 944 | |
| Psychiatric disorders | | | |
| Irritability (IRRITABILITY) | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 863 / 987 (87.44%) | 894 / 1001 (89.31%) | |
| occurrences (all) | 3301 | 3380 | |
| Infections and infestations | | | |
| Otitis media | | | |
| subjects affected / exposed | 50 / 987 (5.07%) | 56 / 1001 (5.59%) | |
| occurrences (all) | 65 | 73 | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 112 / 987 (11.35%) | 114 / 1001 (11.39%) | |
| occurrences (all) | 137 | 137 | |

| | | | |
|---|--------------------|---------------------|--|
| Metabolism and nutrition disorders | | | |
| Decreased appetite (DECREASED APPETITE) | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 492 / 987 (49.85%) | 521 / 1001 (52.05%) | |
| occurrences (all) | 1028 | 1041 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported