



Clinical trial results:

A PHASE 3, RANDOMIZED, DOUBLE-BLIND TRIAL TO EVALUATE THE SAFETY AND IMMUNOGENICITY OF A 20-VALENT PNEUMOCOCCAL CONJUGATE VACCINE GIVEN AS A SERIES OF 2 INFANT DOSES AND 1 TODDLER DOSE IN HEALTHY INFANTS

Summary

| | |
|--------------------------|-------------------------------|
| EudraCT number | 2019-003306-27 |
| Trial protocol | NO CZ EE FI PL SK DK BE NL IT |
| Global end of trial date | 18 February 2023 |

Results information

| | |
|--------------------------------|-------------------|
| Result version number | v1 (current) |
| This version publication date | 01 September 2023 |
| First version publication date | 01 September 2023 |

Trial information

Trial identification

| | |
|-----------------------|----------|
| Sponsor protocol code | B7471012 |
|-----------------------|----------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT04546425 |
| 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 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com |
| Scientific contact | Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 18007181021, ClinicalTrials.gov_Inquiries@pfizer.com |

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

| | |
|--|------------------|
| Analysis stage | Final |
| Date of interim/final analysis | 20 March 2023 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 18 February 2023 |
| 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. Primary immunogenicity objectives for primary study population: Noninferiority (NI) of 20vPnC to 13vPnC based on IgG GMCs at 1 month after Dose 2 and 1 month after Dose 3; Percentage of subjects with predefined IgG concentrations 1 month after Dose 2; NI of percentage of subjects with prespecified antibody levels to specific concomitant vaccine antigens 1 month after Dose 3. Primary immunogenicity objectives for Russian Cohort: to describe IgG responses induced by 20vPnC (Percentages of participants with predefined IgG concentrations at 1 month after Dose 2; IgG GMCs at 1 month after Dose 2 and 1 month after Dose 3)

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 Conference on 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 | 09 September 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 | Australia: 2 |
| Country: Number of subjects enrolled | Belgium: 15 |
| Country: Number of subjects enrolled | Czechia: 72 |
| Country: Number of subjects enrolled | Denmark: 3 |
| Country: Number of subjects enrolled | Estonia: 78 |
| Country: Number of subjects enrolled | Finland: 354 |
| Country: Number of subjects enrolled | Italy: 72 |
| Country: Number of subjects enrolled | Netherlands: 14 |
| Country: Number of subjects enrolled | Norway: 14 |
| Country: Number of subjects enrolled | Poland: 546 |
| Country: Number of subjects enrolled | Slovakia: 34 |
| Country: Number of subjects enrolled | Russian Federation: 51 |
| Worldwide total number of subjects | 1255 |
| EEA total number of subjects | 1202 |

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) | 1255 |
| 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:

For primary study population, 1207 participants were enrolled & assigned to receive 3 doses of 20-valent pneumococcal conjugate vaccine (20vPnC) or 13vPnC of which 3 participants were not vaccinated, 1204 were vaccinated with 20vPnC or 13vPnC. Additional 51 Russian subjects were enrolled, all of which were vaccinated with 20vPnC or 13vPnC.

Period 1

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

Arms

| | |
|------------------------------|----------------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | 20vPnC: Primary Study Population |

Arm description:

Infants 42 to 112 days of age were enrolled to receive 3 doses of 0.5 mL 20vPnC intramuscularly. Dose 1 was given at enrollment and Dose 2 was given 42 to 63 days later. Dose 3 was administered at 335 to 386 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 0.5 mL dose of 20vPnC intramuscularly on Visits 1, 2, and 4 with Dose 1, 2, 3 respectively.

| | |
|------------------|----------------------------------|
| Arm title | 13vPnC: Primary Study Population |
|------------------|----------------------------------|

Arm description:

Infants 42 to 112 days of age were enrolled to receive 3 doses of 0.5 mL 13vPnC intramuscularly. Dose 1 was given at enrollment and Dose 2 was given 42 to 63 days later. Dose 3 was administered at 335 to 386 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 0.5 mL dose of 13vPnC intramuscularly on Visits 1, 2, and 4 with Dose 1, 2, 3 respectively.

| | |
|------------------|------------------------|
| Arm title | 20vPnC: Russian Cohort |
|------------------|------------------------|

Arm description:

Infants 42 to 70 days of age were enrolled to receive 3 doses of 0.5 mL 20vPnC intramuscularly. Dose 1 was given at enrollment and Dose 2 was given 60 to 90 days later. Dose 3 was administered at 335 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 0.5 mL dose of 20vPnC intramuscularly on Visits 1, 2, and 4 with Dose 1, 2, 3 respectively.

| | |
|------------------|------------------------|
| Arm title | 13vPnC: Russian Cohort |
|------------------|------------------------|

Arm description:

Infants 42 to 70 days of age were enrolled to receive 3 doses of 0.5 mL 13vPnC intramuscularly. Dose 1 was given at enrollment and Dose 2 was given 60 to 90 days later. Dose 3 was administered at 335 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 0.5 mL dose of 13vPnC intramuscularly on Visits 1, 2, and 4 with Dose 1, 2, 3 respectively.

| Number of subjects in period 1 | 20vPnC: Primary Study Population | 13vPnC: Primary Study Population | 20vPnC: Russian Cohort |
|------------------------------------|----------------------------------|----------------------------------|------------------------|
| Started | 601 | 603 | 24 |
| Dose 1 | 601 | 603 | 24 |
| Dose 2 | 593 | 598 | 24 |
| Dose 3 | 588 | 594 | 22 |
| Completed | 583 | 590 | 22 |
| Not completed | 18 | 13 | 2 |
| Adverse event, non-fatal | 3 | - | - |
| Lost to follow-up | 5 | 4 | - |
| Withdrawal by parent/guardian | 6 | 5 | 1 |
| Protocol deviation | 1 | 1 | - |
| No Longer met eligibility criteria | 3 | 3 | 1 |

| Number of subjects in period 1 | 13vPnC: Russian Cohort |
|--------------------------------|------------------------|
| Started | 27 |
| Dose 1 | 27 |
| Dose 2 | 27 |
| Dose 3 | 25 |
| Completed | 25 |
| Not completed | 2 |

| | |
|------------------------------------|---|
| Adverse event, non-fatal | - |
| Lost to follow-up | - |
| Withdrawal by parent/guardian | 1 |
| Protocol deviation | - |
| No Longer met eligibility criteria | 1 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|----------------------------------|
| Reporting group title | 20vPnC: Primary Study Population |
|-----------------------|----------------------------------|

Reporting group description:

Infants 42 to 112 days of age were enrolled to receive 3 doses of 0.5 mL 20vPnC intramuscularly. Dose 1 was given at enrollment and Dose 2 was given 42 to 63 days later. Dose 3 was administered at 335 to 386 days of age.

| | |
|-----------------------|----------------------------------|
| Reporting group title | 13vPnC: Primary Study Population |
|-----------------------|----------------------------------|

Reporting group description:

Infants 42 to 112 days of age were enrolled to receive 3 doses of 0.5 mL 13vPnC intramuscularly. Dose 1 was given at enrollment and Dose 2 was given 42 to 63 days later. Dose 3 was administered at 335 to 386 days of age.

| | |
|-----------------------|------------------------|
| Reporting group title | 20vPnC: Russian Cohort |
|-----------------------|------------------------|

Reporting group description:

Infants 42 to 70 days of age were enrolled to receive 3 doses of 0.5 mL 20vPnC intramuscularly. Dose 1 was given at enrollment and Dose 2 was given 60 to 90 days later. Dose 3 was administered at 335 to 455 days of age.

| | |
|-----------------------|------------------------|
| Reporting group title | 13vPnC: Russian Cohort |
|-----------------------|------------------------|

Reporting group description:

Infants 42 to 70 days of age were enrolled to receive 3 doses of 0.5 mL 13vPnC intramuscularly. Dose 1 was given at enrollment and Dose 2 was given 60 to 90 days later. Dose 3 was administered at 335 to 455 days of age.

| Reporting group values | 20vPnC: Primary Study Population | 13vPnC: Primary Study Population | 20vPnC: Russian Cohort |
|--|----------------------------------|----------------------------------|------------------------|
| Number of subjects | 601 | 603 | 24 |
| Age categorical Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 601 | 603 | 24 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 0 | 0 | 0 |
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |
| Age Continuous Units: Days | | | |
| arithmetic mean | 69.2 | 69.7 | 64.2 |
| standard deviation | ± 17.76 | ± 18.32 | ± 6.98 |
| Sex: Female, Male Units: Subjects | | | |
| Female | 302 | 292 | 16 |
| Male | 299 | 311 | 8 |
| Race (NIH/OMB) Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | 0 |
| Asian | 8 | 5 | 0 |

| | | | |
|---|-----|-----|----|
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 |
| Black or African American | 0 | 1 | 0 |
| White | 585 | 592 | 24 |
| More than one race | 1 | 0 | 0 |
| Unknown or Not Reported | 7 | 5 | 0 |
| Ethnicity (NIH/OMB) | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 4 | 1 | 0 |
| Not Hispanic or Latino | 577 | 586 | 22 |
| Unknown or Not Reported | 20 | 16 | 2 |

| Reporting group values | 13vPnC: Russian Cohort | Total | |
|--|------------------------|-------|--|
| Number of subjects | 27 | 1255 | |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | |
| Newborns (0-27 days) | 0 | 0 | |
| Infants and toddlers (28 days-23 months) | 27 | 1255 | |
| Children (2-11 years) | 0 | 0 | |
| Adolescents (12-17 years) | 0 | 0 | |
| Adults (18-64 years) | 0 | 0 | |
| From 65-84 years | 0 | 0 | |
| 85 years and over | 0 | 0 | |
| Age Continuous | | | |
| Units: Days | | | |
| arithmetic mean | 63.3 | | |
| standard deviation | ± 6.21 | - | |
| Sex: Female, Male | | | |
| Units: Subjects | | | |
| Female | 12 | 622 | |
| Male | 15 | 633 | |
| Race (NIH/OMB) | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | |
| Asian | 1 | 14 | |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | |
| Black or African American | 0 | 1 | |
| White | 26 | 1227 | |
| More than one race | 0 | 1 | |
| Unknown or Not Reported | 0 | 12 | |
| Ethnicity (NIH/OMB) | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 0 | 5 | |
| Not Hispanic or Latino | 25 | 1210 | |
| Unknown or Not Reported | 2 | 40 | |

End points

End points reporting groups

| | |
|--|----------------------------------|
| Reporting group title | 20vPnC: Primary Study Population |
| Reporting group description: Infants 42 to 112 days of age were enrolled to receive 3 doses of 0.5 mL 20vPnC intramuscularly. Dose 1 was given at enrollment and Dose 2 was given 42 to 63 days later. Dose 3 was administered at 335 to 386 days of age. | |
| Reporting group title | 13vPnC: Primary Study Population |
| Reporting group description: Infants 42 to 112 days of age were enrolled to receive 3 doses of 0.5 mL 13vPnC intramuscularly. Dose 1 was given at enrollment and Dose 2 was given 42 to 63 days later. Dose 3 was administered at 335 to 386 days of age. | |
| Reporting group title | 20vPnC: Russian Cohort |
| Reporting group description: Infants 42 to 70 days of age were enrolled to receive 3 doses of 0.5 mL 20vPnC intramuscularly. Dose 1 was given at enrollment and Dose 2 was given 60 to 90 days later. Dose 3 was administered at 335 to 455 days of age. | |
| Reporting group title | 13vPnC: Russian Cohort |
| Reporting group description: Infants 42 to 70 days of age were enrolled to receive 3 doses of 0.5 mL 13vPnC intramuscularly. Dose 1 was given at enrollment and Dose 2 was given 60 to 90 days later. Dose 3 was administered at 335 to 455 days of age. | |

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

| | |
|--|--|
| End point title | Percentage of Subjects With Local Reactions Within 7 Days After Dose 1: Primary Study Population ^{[1][2]} |
| End point description: Local reactions included redness, swelling and, pain at the injection site, recorded by parent's/legal guardians of subjects in an electronic diary (e-diary). Redness and swelling were measured and recorded in measuring device units. 1 measuring device unit = 0.5 centimeter (cm). Redness and swelling were graded as mild (greater than [>] 0 to 2.0 cm), moderate (> 2.0 to 7.0 cm) and severe (>7.0 cm). Pain at injection site was graded as mild (hurt if gently touched example, whimpered, winced, protested, or withdrew), moderate (hurt if gently touched, with crying), and severe (caused limitation of limb movement). 95 percent (%) confidence interval (CI) was based on Clopper and Pearson method. Safety analysis set included all subjects who received at least 1 dose of 20vPnC or 13vPnC and had safety data assessed after any dose. Here, "Number of subjects Analyzed" signifies the number of subjects with any e-diary data after Dose 1. | |
| End point type | Primary |
| End point timeframe: Within 7 days after Dose 1 | |
| Notes: [1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. Justification: This endpoint was planned to be analysed only for the specified reporting arms [2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Only descriptive analysis was planned for this endpoint | |

| End point values | 20vPnC: Primary Study Population | 13vPnC: Primary Study Population | | |
|----------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 598 | 603 | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Redness: Mild | 20.7 (17.6 to 24.2) | 22.7 (19.4 to 26.3) | | |
| Redness: Moderate | 4.5 (3.0 to 6.5) | 4.8 (3.2 to 6.8) | | |
| Redness: Severe | 0 (0.0 to 0.6) | 0 (0.0 to 0.6) | | |
| Swelling: Mild | 12.7 (10.1 to 15.6) | 12.9 (10.4 to 15.9) | | |
| Swelling: Moderate | 8.7 (6.6 to 11.2) | 7.3 (5.4 to 9.7) | | |
| Swelling: Severe | 0 (0.0 to 0.6) | 0 (0.0 to 0.6) | | |
| Pain at Injection Site: Mild | 16.7 (13.8 to 20.0) | 17.9 (14.9 to 21.2) | | |
| Pain at Injection Site: Moderate | 12.0 (9.5 to 14.9) | 11.4 (9.0 to 14.3) | | |
| Pain at Injection Site: Severe | 0.3 (0.0 to 1.2) | 0 (0.0 to 0.6) | | |

Statistical analyses

No statistical analyses for this end point

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

| | |
|-----------------|--|
| End point title | Percentage of Subjects With Local Reactions Within 7 Days After Dose 2: Primary Study Population ^{[3][4]} |
|-----------------|--|

End point description:

Local reactions included redness, swelling and, pain at the injection site, recorded by parent's/legal guardians of subjects in an e-diary. Redness and swelling were measured and recorded in measuring device units. 1 measuring device unit = 0.5 cm. Redness and swelling were graded as mild (>0 to 2.0 cm), moderate (> 2.0 to 7.0 cm) and severe (>7.0 cm). Pain at injection site was graded as mild (hurt if gently touched example, whimpered, winced, protested, or withdrew), moderate (hurt if gently touched, with crying), and severe (caused limitation of limb movement). 95% CI was based on Clopper and Pearson method. Safety analysis set included all subjects who received at least 1 dose of 20vPnC or 13vPnC and had safety data assessed after any dose. Here, "Number of Subjects Analyzed" signifies the number of subjects with any e-diary data after Dose 2.

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

End point timeframe:

Within 7 days after Dose 2

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

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

Justification: Only descriptive analysis was planned for this endpoint

| End point values | 20vPnC: Primary Study Population | 13vPnC: Primary Study Population | | |
|----------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 592 | 594 | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Redness: Mild | 24.8 (21.4 to 28.5) | 22.9 (19.6 to 26.5) | | |
| Redness: Moderate | 3.7 (2.3 to 5.6) | 5.1 (3.4 to 7.1) | | |
| Redness: Severe | 0 (0.0 to 0.6) | 0.2 (0.0 to 0.9) | | |
| Swelling: Mild | 13.7 (11.0 to 16.7) | 14.1 (11.4 to 17.2) | | |
| Swelling: Moderate | 8.3 (6.2 to 10.8) | 6.2 (4.4 to 8.5) | | |
| Swelling: Severe | 0 (0.0 to 0.6) | 0.2 (0.0 to 0.9) | | |
| Pain at Injection Site: Mild | 13.3 (10.7 to 16.4) | 16.5 (13.6 to 19.7) | | |
| Pain at Injection Site: Moderate | 9.3 (7.1 to 11.9) | 7.9 (5.9 to 10.4) | | |
| Pain at Injection Site: Severe | 0.2 (0.0 to 0.9) | 0.2 (0.0 to 0.9) | | |

Statistical analyses

No statistical analyses for this end point

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

| | |
|-----------------|--|
| End point title | Percentage of Subjects With Local Reactions Within 7 Days After Dose 3: Primary Study Population ^[5] ^[6] |
|-----------------|--|

End point description:

Local reactions included redness, swelling and, pain at the injection site, recorded by parent's/legal guardians of subjects in an e-diary. Redness and swelling were measured and recorded in measuring device units. 1 measuring device unit = 0.5 cm. Redness and swelling were graded as mild (>0 to 2.0 cm), moderate (> 2.0 to 7.0 cm) and severe (>7.0 cm). Pain at injection site was graded as mild (hurt if gently touched example, whimpered, winced, protested, or withdrew), moderate (hurt if gently touched, with crying), and severe (caused limitation of limb movement). 95% CI was based on Clopper and Pearson method. Safety analysis set included all subjects who received at least 1 dose of 20vPnC or 13vPnC and had safety data assessed after any dose. Here, "Number of Subjects Analyzed" signifies the number of subjects with any e-diary data after Dose 3.

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

End point timeframe:

Within 7 days after Dose 3

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

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

Justification: Only descriptive analysis was planned for this endpoint

| End point values | 20vPnC: Primary Study Population | 13vPnC: Primary Study Population | | |
|----------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 580 | 586 | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Redness: Mild | 23.3 (19.9 to 26.9) | 25.1 (21.6 to 28.8) | | |
| Redness: Moderate | 13.4 (10.8 to 16.5) | 8.5 (6.4 to 11.1) | | |
| Redness: Severe | 0.2 (0.0 to 1.0) | 0.2 (0.0 to 0.9) | | |
| Swelling: Mild | 17.8 (14.7 to 21.1) | 14.5 (11.8 to 17.6) | | |
| Swelling: Moderate | 11.9 (9.4 to 14.8) | 9.7 (7.5 to 12.4) | | |
| Swelling: Severe | 0.2 (0.0 to 1.0) | 0.3 (0.0 to 1.2) | | |
| Pain at Injection Site: Mild | 24.7 (21.2 to 28.4) | 22.4 (19.0 to 25.9) | | |
| Pain at Injection Site: Moderate | 17.4 (14.4 to 20.8) | 17.2 (14.3 to 20.5) | | |
| Pain at Injection Site: Severe | 0.3 (0.0 to 1.2) | 0.3 (0.0 to 1.2) | | |

Statistical analyses

No statistical analyses for this end point

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

| | |
|-----------------|--|
| End point title | Percentage of Subjects With Systemic Events Within 7 Days After Dose 1: Primary Study Population ^{[7][8]} |
|-----------------|--|

End point description:

Systemic events: fever, decreased appetite, drowsiness/increased sleep & irritability, recorded by parents/legal guardians of subjects using e-diary. Fever: temperature ≥ 38.0 degree C & categorized as ≥ 38.0 to 38.4 degree C, >38.4 to 38.9 degree C, >38.9 to 40.0 degree C & >40.0 -degree C. Decreased appetite: mild (decreased interest in eating), moderate (decreased oral intake) & severe (refusal to feed). Drowsiness was graded as mild (increased/prolonged sleeping bouts), moderate (slightly subdued, interfered with daily activity) & severe (disabling, not interested in usual daily activity). Irritability: mild (easily consolable), moderate (required increased attention) & severe (inconsolable, crying could not be comforted). 95% CI was based on Clopper & Pearson method. Safety analysis set: all subjects who received at least 1 dose of 20vPnC or 13vPnC & had safety data assessed after any dose. Here, "Number of Subjects Analyzed": number of subjects with any e-diary data after Dose 1

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

End point timeframe:

Within 7 Days after Dose 1

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

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

Justification: Only descriptive analysis was planned for this endpoint

| End point values | 20vPnC: Primary Study Population | 13vPnC: Primary Study Population | | |
|--|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 598 | 603 | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Fever: ≥ 38.0 degrees C to 38.4 degrees C | 7.5 (5.5 to 9.9) | 6.8 (4.9 to 9.1) | | |
| Fever: > 38.4 degrees C to 38.9 degrees C | 1.3 (0.6 to 2.6) | 1.3 (0.6 to 2.6) | | |
| Fever: > 38.9 degrees C to 40.0 degrees C | 0 (0.0 to 0.6) | 0.3 (0.0 to 1.2) | | |
| Fever: > 40.0 degrees C | 0 (0.0 to 0.6) | 0 (0.0 to 0.6) | | |
| Decreased appetite: Mild | 16.2 (13.4 to 19.4) | 13.3 (10.7 to 16.2) | | |
| Decreased appetite: Moderate | 7.5 (5.5 to 9.9) | 8.8 (6.7 to 11.3) | | |
| Decreased appetite: Severe | 1.0 (0.4 to 2.2) | 0.5 (0.1 to 1.4) | | |
| Drowsiness: Mild | 46.0 (41.9 to 50.1) | 48.6 (44.5 to 52.7) | | |
| Drowsiness: Moderate | 14.4 (11.7 to 17.5) | 14.3 (11.6 to 17.3) | | |
| Drowsiness: Severe | 0.8 (0.3 to 1.9) | 0.8 (0.3 to 1.9) | | |
| Irritability: Mild | 17.6 (14.6 to 20.8) | 17.4 (14.5 to 20.7) | | |
| Irritability: Moderate | 46.2 (42.1 to 50.2) | 46.4 (42.4 to 50.5) | | |
| Irritability: Severe | 8.2 (6.1 to 10.7) | 8.6 (6.5 to 11.2) | | |

Statistical analyses

No statistical analyses for this end point

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

| | |
|--|---|
| End point title | Percentage of Subjects With Systemic Events Within 7 Days After Dose 2: Primary Study Population ^{[9][10]} |
| End point description: Systemic events: fever, decreased appetite, drowsiness/increased sleep & irritability, recorded by parents/legal guardians of subject's using e-diary. Fever: temperature ≥ 38.0 degree C & categorized as ≥ 38.0 to 38.4 degree C, > 38.4 to 38.9 degree C, > 38.9 to 40.0 degree C & > 40.0 -degree C. Decreased appetite: mild (decreased interest in eating), moderate (decreased oral intake) & severe (refusal to feed). Drowsiness was graded as mild (increased/prolonged sleeping bouts), moderate (slightly subdued, interfered with daily activity) & severe (disabling, not interested in usual daily activity). Irritability: mild (easily consolable), moderate (required increased attention) & severe (inconsolable, crying could not be comforted). 95% CI was based on Clopper & Pearson method. Safety analysis set: all subjects who received at least 1 dose of 20vPnC or 13vPnC & had safety data assessed after any dose. Here, "Number of Subjects Analyzed": number of subjects with any e-diary data after Dose2 | |
| End point type | Primary |
| End point timeframe: Within 7 Days after Dose 2 | |

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 analysis was planned for this endpoint

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

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

| End point values | 20vPnC: Primary Study Population | 13vPnC: Primary Study Population | | |
|--|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 592 | 594 | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Fever: ≥ 38.0 degrees C to 38.4 degrees C | 11.7 (9.2 to 14.5) | 11.6 (9.2 to 14.5) | | |
| Fever: >38.4 degrees C to 38.9 degrees C | 2.5 (1.4 to 4.1) | 2.0 (1.0 to 3.5) | | |
| Fever: >38.9 degrees C to 40.0 degrees C | 0.7 (0.2 to 1.7) | 0.3 (0.0 to 1.2) | | |
| Fever: >40.0 degrees C | 0 (0.0 to 0.6) | 0 (0.0 to 0.6) | | |
| Decreased appetite: Mild | 13.5 (10.9 to 16.5) | 12.1 (9.6 to 15.0) | | |
| Decreased appetite: Moderate | 10.1 (7.8 to 12.9) | 6.4 (4.6 to 8.7) | | |
| Decreased appetite: Severe | 1.0 (0.4 to 2.2) | 0.8 (0.3 to 2.0) | | |
| Drowsiness: Mild | 37.8 (33.9 to 41.9) | 37.0 (33.1 to 41.1) | | |
| Drowsiness: Moderate | 13.2 (10.6 to 16.2) | 13.5 (10.8 to 16.5) | | |
| Drowsiness: Severe | 0.3 (0.0 to 1.2) | 0.2 (0.0 to 0.9) | | |
| Irritability: Mild | 22.8 (19.5 to 26.4) | 21.2 (18.0 to 24.7) | | |
| Irritability: Moderate | 43.1 (39.0 to 47.2) | 40.6 (36.6 to 44.6) | | |
| Irritability: Severe | 5.7 (4.0 to 7.9) | 6.6 (4.7 to 8.9) | | |

Statistical analyses

No statistical analyses for this end point

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

| | |
|-----------------|--|
| End point title | Percentage of Subjects With Systemic Events Within 7 Days After Dose 3: Primary Study Population ^{[11][12]} |
|-----------------|--|

End point description:

Systemic events: fever, decreased appetite, drowsiness/increased sleep & irritability, recorded by parents/legal guardians of subject's using e-diary. Fever: temperature ≥ 38.0 degree C & categorized as ≥ 38.0 to 38.4 degree C, >38.4 to 38.9 degree C, >38.9 to 40.0 degree C & >40.0 -degree C. Decreased appetite: mild (decreased interest in eating), moderate (decreased oral intake) & severe (refusal to feed). Drowsiness was graded as mild (increased/prolonged sleeping bouts), moderate (slightly subdued, interfered with daily activity) & severe (disabling, not interested in usual daily activity). Irritability: mild (easily consolable), moderate (required increased attention) & severe (inconsolable, crying could not be comforted). 95% CI was based on Clopper & Pearson method. Safety analysis set: all subjects who received at least 1 dose of 20vPnC or 13vPnC & had safety data assessed

after any dose. Here, "Number of Subjects Analyzed": number of subjects with any e-diary data after Dose 3.

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

End point timeframe:

Within 7 Days after Dose 3

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 analysis was planned for this endpoint

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

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

| End point values | 20vPnC: Primary Study Population | 13vPnC: Primary Study Population | | |
|--|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 580 | 586 | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Fever: ≥ 38.0 degrees C to 38.4 degrees C | 13.4 (10.8 to 16.5) | 13.5 (10.8 to 16.5) | | |
| Fever: > 38.4 degrees C to 38.9 degrees C | 6.9 (5.0 to 9.3) | 7.0 (5.1 to 9.4) | | |
| Fever: > 38.9 degrees C to 40.0 degrees C | 3.6 (2.3 to 5.5) | 3.2 (2.0 to 5.0) | | |
| Fever: > 40.0 degrees C | 0.3 (0.0 to 1.2) | 0 (0.0 to 0.6) | | |
| Decreased appetite: Mild | 20.0 (16.8 to 23.5) | 15.5 (12.7 to 18.7) | | |
| Decreased appetite: Moderate | 17.1 (14.1 to 20.4) | 18.9 (15.8 to 22.4) | | |
| Decreased appetite: Severe | 2.2 (1.2 to 3.8) | 2.0 (1.1 to 3.5) | | |
| Drowsiness: Mild | 34.8 (30.9 to 38.9) | 32.8 (29.0 to 36.7) | | |
| Drowsiness: Moderate | 15.3 (12.5 to 18.5) | 14.7 (11.9 to 17.8) | | |
| Drowsiness: Severe | 0.7 (0.2 to 1.8) | 1.2 (0.5 to 2.4) | | |
| Irritability: Mild | 23.4 (20.1 to 27.1) | 21.3 (18.1 to 24.9) | | |
| Irritability: Moderate | 43.4 (39.4 to 47.6) | 45.4 (41.3 to 49.5) | | |
| Irritability: Severe | 4.1 (2.7 to 6.1) | 4.1 (2.6 to 6.0) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Serious Adverse Events (SAEs) From Dose 1 to 1 Month After Dose 3: Primary Study Population

| | |
|-----------------|---|
| End point title | Percentage of Subjects With Serious Adverse Events (SAEs) From Dose 1 to 1 Month After Dose 3: Primary Study Population ^{[13][14]} |
|-----------------|---|

End point description:

An SAE was any untoward medical occurrence that occurred, at any dose: resulted in death; required

inpatient hospitalization or prolongation of existing hospitalization; was life-threatening; resulted in persistent or significant disability/ incapacity; was a congenital anomaly/birth defect and other important medical events. 95% CI was based on the Clopper and Pearson method. Safety analysis set included all subjects who received at least 1 dose of 20vPnC or 13vPnC and had safety data assessed after any dose.

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

End point timeframe:

From Dose 1 to 1 month after Dose 3

Notes:

[13] - 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 analysis was planned for this endpoint

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

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

| End point values | 20vPnC: Primary Study Population | 13vPnC: Primary Study Population | | |
|----------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 601 | 603 | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | 5.7 (3.9 to 7.8) | 6.6 (4.8 to 8.9) | | |

Statistical analyses

No statistical analyses for this end point

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

| | |
|-----------------|--|
| End point title | Percentage of Subjects With Adverse Events (AEs) From Dose 3 to 1 Month After Dose 3: Primary Study Population ^{[15][16]} |
|-----------------|--|

End point description:

An AE was any untoward medical occurrence in a subject, temporally associated with the use of study treatment, whether or not considered related to the study treatment. 95% CI was based on the Clopper and Pearson method. AEs reported in this outcome measure excluded local reactions and systemic events collected from e-diary. Safety analysis set included all subjects who received at least 1 dose of 20vPnC or 13vPnC and had safety data assessed after any dose. Here, "Number of Subjects Analyzed" signifies the number of subjects who received Dose 3.

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

End point timeframe:

From Dose 3 to 1 month after Dose 3

Notes:

[15] - 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 analysis was planned for this endpoint

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

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

| End point values | 20vPnC: Primary Study Population | 13vPnC: Primary Study Population | | |
|----------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 588 | 594 | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | 15.5 (12.6 to 18.7) | 16.5 (13.6 to 19.7) | | |

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 2: Primary Study Population

| | |
|-----------------|--|
| End point title | Percentage of Subjects With Adverse Events (AEs) From Dose 1 to 1 Month After Dose 2: Primary Study Population ^{[17][18]} |
|-----------------|--|

End point description:

An AE was any untoward medical occurrence in a subject, temporally associated with the use of study treatment, whether or not considered related to the study treatment. 95% CI was based on the Clopper and Pearson method. AEs reported in this outcome measure excluded local reactions and systemic events collected from e-diary. Safety analysis set included all subjects who received at least 1 dose of 20vPnC or 13vPnC and had safety data assessed after any dose.

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

End point timeframe:

From Dose 1 to 1 month after Dose 2

Notes:

[17] - 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 analysis was planned for this endpoint

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

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

| End point values | 20vPnC: Primary Study Population | 13vPnC: Primary Study Population | | |
|----------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 601 | 603 | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | 13.8 (11.2 to 16.8) | 14.4 (11.7 to 17.5) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Newly Diagnosed Chronic Medical Condition (NDCMC) From Dose 1 to 1 Month After Dose 3: Primary Study Population

| | |
|-----------------|--|
| End point title | Percentage of Subjects With Newly Diagnosed Chronic Medical Condition (NDCMC) From Dose 1 to 1 Month After Dose 3: |
|-----------------|--|

End point description:

An NDCMC was defined as a disease or medical condition, not previously identified, that was expected to be persistent or was otherwise long-lasting in its effects. 95% CI was based on the Clopper and Pearson method. Safety analysis set included all subjects who received at least 1 dose of 20vPnC or 13vPnC and had safety data assessed after any dose.

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

End point timeframe:

From Dose 1 to 1 month after Dose 3

Notes:

[19] - 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: This endpoint was planned to be analysed only for the specified reporting arms

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

Justification: Only descriptive analysis was planned for this endpoint

| End point values | 20vPnC: Primary Study Population | 13vPnC: Primary Study Population | | |
|----------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 601 | 603 | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | 1.0 (0.4 to 2.2) | 1.0 (0.4 to 2.2) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Predefined Pneumococcal Immunoglobulin G (IgG) Antibody 1 Month After Dose 2: Primary Study Population

| | |
|-----------------|--|
| End point title | Percentage of Subjects With Predefined Pneumococcal Immunoglobulin G (IgG) Antibody 1 Month After Dose 2: Primary Study Population ^[21] |
|-----------------|--|

End point description:

Predefined IgG concentrations 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. 95% CI was based on the Clopper and Pearson method. Dose 2 evaluable immunogenicity population: eligible subjects 42-112 days of age at first vaccination, received first 2 doses as randomized, at least 1 valid immunogenicity results from blood collection (27 to 56 days after Dose 2), no other major protocol deviations. "Number of Subjects Analyzed"= subjects in Dose 2 evaluable immunogenicity population, "n"= subjects with valid IgG assay results for specified serotype.

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

End point timeframe:

1 month after Dose 2

Notes:

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

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

| End point values | 20vPnC: Primary Study Population | 13vPnC: Primary Study Population | | |
|----------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 567 | 562 | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Serotype 1, n=566, 562 | 70.7 (66.7 to 74.4) | 84.2 (80.9 to 87.1) | | |
| Serotype 3, n=566, 562 | 58.0 (53.8 to 62.1) | 75.8 (72.0 to 79.3) | | |
| Serotype 4, n=566, 562 | 68.6 (64.5 to 72.4) | 79.5 (76.0 to 82.8) | | |
| Serotype 5, n=566, 562 | 63.4 (59.3 to 67.4) | 76.0 (72.2 to 79.5) | | |
| Serotype 6A, n=566, 562 | 59.5 (55.4 to 63.6) | 73.7 (69.8 to 77.3) | | |
| Serotype 6B, n=564, 561 | 20.7 (17.5 to 24.3) | 36.5 (32.5 to 40.7) | | |
| Serotype 7F, n=566, 562 | 87.6 (84.6 to 90.2) | 90.2 (87.5 to 92.5) | | |
| Serotype 9V, n=566, 562 | 60.2 (56.1 to 64.3) | 74.6 (70.7 to 78.1) | | |
| Serotype 14, n=565, 562 | 78.6 (75.0 to 81.9) | 81.9 (78.4 to 85.0) | | |
| Serotype 18C, n=566, 562 | 71.0 (67.1 to 74.7) | 76.5 (72.8 to 80.0) | | |
| Serotype 19A, n=566, 562 | 92.2 (89.7 to 94.3) | 94.0 (91.6 to 95.8) | | |
| Serotype 19F, n=566, 562 | 94.3 (92.1 to 96.1) | 95.7 (93.7 to 97.2) | | |
| Serotype 23F, n=566, 562 | 23.5 (20.1 to 27.2) | 41.8 (37.7 to 46.0) | | |
| Serotype 8, n=567, 561 | 96.5 (94.6 to 97.8) | 2.9 (1.6 to 4.6) | | |
| Serotype 10A, n=567, 562 | 28.9 (25.2 to 32.8) | 2.7 (1.5 to 4.4) | | |
| Serotype 11A, n=567, 562 | 94.2 (91.9 to 96.0) | 2.0 (1.0 to 3.5) | | |
| Serotype 12F, n=567, 562 | 30.3 (26.6 to 34.3) | 0.2 (0.0 to 1.0) | | |
| Serotype 15B, n=566, 562 | 94.3 (92.1 to 96.1) | 8.5 (6.4 to 11.2) | | |
| Serotype 22F, n=567, 562 | 94.4 (92.1 to 96.1) | 2.0 (1.0 to 3.5) | | |
| Serotype 33F, n=566, 562 | 46.8 (42.6 to 51.0) | 2.7 (1.5 to 4.4) | | |

Statistical analyses

| | |
|--|---|
| Statistical analysis title | 20vPnC Versus 13vPnC |
| Statistical analysis description: | |
| Serotype 4: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage. | |
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |

| | |
|---|--------------------|
| Number of subjects included in analysis | 1129 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Percent Difference |
| Point estimate | -11 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -16 |
| upper limit | -5.9 |

| | |
|---|---|
| Statistical analysis title | 20vPnC Versus 13vPnC |
| Statistical analysis description: Serotype 3: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage. | |
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1129 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Percent Difference |
| Point estimate | -17.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -23.2 |
| upper limit | -12.4 |

| | |
|---|---|
| Statistical analysis title | 20vPnC Versus 13vPnC |
| Statistical analysis description: Serotype 5: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage. | |
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1129 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Percent Difference |
| Point estimate | -12.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -17.8 |
| upper limit | -7.2 |

| | |
|--|---|
| Statistical analysis title | 20vPnC Versus 13vPnC |
| Statistical analysis description: | |
| Serotype 1: 2-Sided 95% CIs are calculated using the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage. | |
| Comparison groups | 13vPnC: Primary Study Population v 20vPnC: Primary Study Population |
| Number of subjects included in analysis | 1129 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Percent Difference |
| Point estimate | -13.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -18.3 |
| upper limit | -8.7 |

| | |
|---|---|
| Statistical analysis title | 20vPnC Versus 13vPnC |
| Statistical analysis description: | |
| Serotype 7F: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage. | |
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1129 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Percent Difference |
| Point estimate | -2.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -6.3 |
| upper limit | 1.1 |

| | |
|---|---|
| Statistical analysis title | 20vPnC Versus 13vPnC |
| Statistical analysis description: | |
| Serotype 6A: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage. | |
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1129 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Percent Difference |
| Point estimate | -14.1 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -19.5 |
| upper limit | -8.6 |

| | |
|-----------------------------------|----------------------|
| Statistical analysis title | 20vPnC Versus 13vPnC |
|-----------------------------------|----------------------|

Statistical analysis description:

Serotype 9V: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage.

| | |
|---|---|
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1129 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Percent Difference |
| Point estimate | -14.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -19.7 |
| upper limit | -8.9 |

| | |
|-----------------------------------|----------------------|
| Statistical analysis title | 20vPnC Versus 13vPnC |
|-----------------------------------|----------------------|

Statistical analysis description:

Serotype 6B: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage.

| | |
|---|---|
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1129 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Percent Difference |
| Point estimate | -15.8 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -21 |
| upper limit | -10.6 |

| | |
|-----------------------------------|----------------------|
| Statistical analysis title | 20vPnC Versus 13vPnC |
|-----------------------------------|----------------------|

Statistical analysis description:

Serotype 19A: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage.

| | |
|-------------------|---|
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
|-------------------|---|

| | |
|---|--------------------|
| Number of subjects included in analysis | 1129 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Percent Difference |
| Point estimate | -1.7 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -4.8 |
| upper limit | 1.3 |

| | |
|--|---|
| Statistical analysis title | 20vPnC Versus 13vPnC |
| Statistical analysis description: | |
| Serotype 19F: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage. | |
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1129 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Percent Difference |
| Point estimate | -1.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -4 |
| upper limit | 1.2 |

| | |
|--|---|
| Statistical analysis title | 20vPnC Versus 13vPnC |
| Statistical analysis description: | |
| Serotype 23F: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage. | |
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1129 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Percent Difference |
| Point estimate | -18.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -23.6 |
| upper limit | -12.9 |

| | |
|---|---|
| Statistical analysis title | 20vPnC Versus 13vPnC |
| Statistical analysis description: Serotype 8: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage. | |
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1129 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Percent difference |
| Point estimate | 59.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 55.6 |
| upper limit | 64.1 |

| | |
|--|---|
| Statistical analysis title | 20vPnC Versus 13vPnC |
| Statistical analysis description: Serotype 10A: 2-Sided 95% CI based on the Percent difference for the difference in proportions expressed as a percentage. | |
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1129 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Percent difference |
| Point estimate | -7.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -13.1 |
| upper limit | -2.1 |

| | |
|--|---|
| Statistical analysis title | 20vPnC Versus 13vPnC |
| Statistical analysis description: Serotype 14: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage. | |
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1129 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Percent Difference |
| Point estimate | -3.3 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -7.9 |
| upper limit | 1.4 |

| | |
|-----------------------------------|----------------------|
| Statistical analysis title | 20vPnC Versus 13vPnC |
|-----------------------------------|----------------------|

Statistical analysis description:

Serotype 18C: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage.

| | |
|---|---|
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1129 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Percent Difference |
| Point estimate | -5.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -10.6 |
| upper limit | -0.4 |

| | |
|-----------------------------------|----------------------|
| Statistical analysis title | 20vPnC Versus 13vPnC |
|-----------------------------------|----------------------|

Statistical analysis description:

Serotype 11A: 2-Sided 95% CI based on the Percent difference for the difference in proportions expressed as a percentage.

| | |
|---|---|
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1129 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Percent difference |
| Point estimate | 57.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 53.1 |
| upper limit | 61.9 |

| | |
|-----------------------------------|----------------------|
| Statistical analysis title | 20vPnC Versus 13vPnC |
|-----------------------------------|----------------------|

Statistical analysis description:

Serotype 22F: 2-Sided 95% CI based on the Percent difference for the difference in proportions expressed as a percentage.

| | |
|-------------------|---|
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
|-------------------|---|

| | |
|---|--------------------|
| Number of subjects included in analysis | 1129 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Percent difference |
| Point estimate | 57.8 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 53.3 |
| upper limit | 62.1 |

| | |
|--|---|
| Statistical analysis title | 20vPnC Versus 13vPnC |
| Statistical analysis description: Serotype 33F: 2-Sided 95% CI based on the Percent difference for the difference in proportions expressed as a percentage. | |
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1129 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Percent difference |
| Point estimate | 10.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 4.5 |
| upper limit | 16 |

| | |
|--|---|
| Statistical analysis title | 20vPnC Versus 13vPnC |
| Statistical analysis description: Serotype 12F: 2-Sided 95% CI based on the Percent difference for the difference in proportions expressed as a percentage. | |
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1129 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Percent difference |
| Point estimate | -6.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -11.7 |
| upper limit | -0.7 |

| | |
|--|---|
| Statistical analysis title | 20vPnC Versus 13vPnC |
| Statistical analysis description: Serotype 15B: 2-Sided 95% CI based on the Percent difference for the difference in proportions expressed as a percentage. | |
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1129 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Percent difference |
| Point estimate | 57.8 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 53.3 |
| upper limit | 62.1 |

Primary: Geometric Mean Concentration (GMC) of Serotype-specific Pneumococcal IgG Antibody 1 Month After Dose 2: Primary Study Population

| | |
|-----------------|--|
| End point title | Geometric Mean Concentration (GMC) of Serotype-specific Pneumococcal IgG Antibody 1 Month After Dose 2: Primary Study Population ^[22] |
|-----------------|--|

End point description:

Pneumococcal serotype-specific IgG concentration was measured for serum sample for 13vPnC serotype: 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F, 7 additional serotype: 8, 10A, 11A, 12F, 15B, 22F, 33F. GMC & corresponding 2-sided 95% CIs were calculated by exponentiating mean logarithm of concentration, corresponding 2-sided 95% CIs (based on Student's t distribution). Assay result below LLOQ was set to 0.5 × LLOQ. GMRs were reported in statistical analysis section & were calculated by exponentiating mean difference of logarithm of concentration & corresponding 2-sided 95% CIs (based on Student's t distribution). Dose 2 evaluable immunogenicity population: eligible subject 42-112 days of age at first vaccination, received 1st 2 doses as randomized, at least 1 valid immunogenicity result from blood collection (27-56 days after Dose2). "Number of Subject Analyzed" = subject in Dose 2 evaluable immunogenicity population, "n" = subject with valid IgG assay result for specified serotype.

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

End point timeframe:

1 month after Dose 2

Notes:

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

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

| End point values | 20vPnC: Primary Study Population | 13vPnC: Primary Study Population | | |
|--|----------------------------------|----------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 567 | 562 | | |
| Units: mcg/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Serotype 1, n=566, 562 | 0.57 (0.52 to 0.62) | 0.93 (0.86 to 1.01) | | |
| Serotype 3, n=566, 562 | 0.41 (0.38 to 0.45) | 0.58 (0.54 to 0.63) | | |

| | | | | |
|--------------------------|---------------------|---------------------|--|--|
| Serotype 4, n=566, 562 | 0.55 (0.50 to 0.61) | 0.92 (0.83 to 1.02) | | |
| Serotype 5, n=566, 562 | 0.34 (0.30 to 0.38) | 0.56 (0.50 to 0.62) | | |
| Serotype 6A, n=566, 562 | 0.45 (0.40 to 0.52) | 0.84 (0.73 to 0.95) | | |
| Serotype 6B, n=564, 561 | 0.03 (0.03 to 0.04) | 0.06 (0.05 to 0.07) | | |
| Serotype 7F, n=566, 562 | 1.02 (0.94 to 1.10) | 1.41 (1.30 to 1.53) | | |
| Serotype 9V, n=566, 562 | 0.45 (0.40 to 0.51) | 0.77 (0.68 to 0.87) | | |
| Serotype 14, n=565, 562 | 1.05 (0.94 to 1.18) | 1.28 (1.14 to 1.43) | | |
| Serotype 18C, n=566, 562 | 0.69 (0.62 to 0.77) | 0.87 (0.78 to 0.98) | | |
| Serotype 19A, n=566, 562 | 0.67 (0.61 to 0.74) | 1.13 (1.01 to 1.26) | | |
| Serotype 19F, n=566, 562 | 2.21 (2.04 to 2.40) | 3.06 (2.80 to 3.34) | | |
| Serotype 23F, n=566, 562 | 0.13 (0.12 to 0.15) | 0.25 (0.22 to 0.28) | | |
| Serotype 8, n=567, 561 | 1.62 (1.51 to 1.74) | 0.02 (0.02 to 0.02) | | |
| Serotype 10A, n=567, 562 | 0.16 (0.14 to 0.18) | 0.02 (0.02 to 0.02) | | |
| Serotype 11A, n=567, 562 | 1.62 (1.50 to 1.75) | 0.02 (0.02 to 0.02) | | |
| Serotype 12F, n=567, 562 | 0.15 (0.13 to 0.17) | 0.01 (0.01 to 0.01) | | |
| Serotype 15B, n=566, 562 | 3.33 (3.00 to 3.70) | 0.04 (0.04 to 0.04) | | |
| Serotype 22F, n=567, 562 | 2.25 (2.06 to 2.45) | 0.01 (0.01 to 0.01) | | |
| Serotype 33F, n=566, 562 | 0.31 (0.28 to 0.34) | 0.03 (0.02 to 0.03) | | |

Statistical analyses

| Statistical analysis title | 20vPnC Versus 13vPnC |
|--|---|
| Statistical analysis description: | |
| Serotype 4: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations. | |
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1129 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 0.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.52 |
| upper limit | 0.69 |

| | |
|---|---|
| Statistical analysis title | 20vPnC Versus 13vPnC |
| Statistical analysis description: Serotype 3: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations. | |
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1129 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 0.71 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.64 |
| upper limit | 0.79 |

| | |
|---|---|
| Statistical analysis title | 20vPnC Versus 13vPnC |
| Statistical analysis description: Serotype 1: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations. | |
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1129 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 0.61 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.54 |
| upper limit | 0.69 |

| | |
|--|---|
| Statistical analysis title | 20vPnC Versus 13vPnC |
| Statistical analysis description: Serotype 9V: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations. | |
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |

| | |
|---|----------------------|
| Number of subjects included in analysis | 1129 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 0.59 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.5 |
| upper limit | 0.69 |

| | |
|-----------------------------------|----------------------|
| Statistical analysis title | 20vPnC Versus 13vPnC |
|-----------------------------------|----------------------|

Statistical analysis description:

Serotype 7F: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations.

| | |
|---|---|
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1129 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 0.72 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.64 |
| upper limit | 0.8 |

| | |
|-----------------------------------|----------------------|
| Statistical analysis title | 20vPnC Versus 13vPnC |
|-----------------------------------|----------------------|

Statistical analysis description:

Serotype 6B: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations.

| | |
|---|---|
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1129 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 0.51 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.43 |
| upper limit | 0.61 |

| | |
|--|---|
| Statistical analysis title | 20vPnC Versus 13vPnC |
| Statistical analysis description: Serotype 6A: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations. | |
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1129 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 0.54 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.45 |
| upper limit | 0.65 |

| | |
|---|---|
| Statistical analysis title | 20vPnC Versus 13vPnC |
| Statistical analysis description: Serotype 5: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations. | |
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1129 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 0.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.52 |
| upper limit | 0.7 |

| | |
|---|---|
| Statistical analysis title | 20vPnC Versus 13vPnC |
| Statistical analysis description: Serotype 12F: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations. | |
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1129 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 2.48 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 2.08 |
| upper limit | 2.97 |

| | |
|-----------------------------------|----------------------|
| Statistical analysis title | 20vPnC Versus 13vPnC |
|-----------------------------------|----------------------|

Statistical analysis description:

Serotype 15B: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations.

| | |
|---|---|
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1129 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 54.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 46.35 |
| upper limit | 64.3 |

| | |
|-----------------------------------|----------------------|
| Statistical analysis title | 20vPnC Versus 13vPnC |
|-----------------------------------|----------------------|

Statistical analysis description:

Serotype 22F: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations.

| | |
|---|---|
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1129 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 36.8 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 31.57 |
| upper limit | 42.89 |

| | |
|-----------------------------------|----------------------|
| Statistical analysis title | 20vPnC Versus 13vPnC |
|-----------------------------------|----------------------|

Statistical analysis description:

Serotype 11A: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations.

| | |
|-------------------|---|
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
|-------------------|---|

| | |
|---|----------------------|
| Number of subjects included in analysis | 1129 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 26.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 22.95 |
| upper limit | 30.82 |

| | |
|-----------------------------------|----------------------|
| Statistical analysis title | 20vPnC Versus 13vPnC |
|-----------------------------------|----------------------|

Statistical analysis description:

Serotype 10A: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations.

| | |
|---|---|
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1129 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 2.67 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 2.25 |
| upper limit | 3.17 |

| | |
|-----------------------------------|----------------------|
| Statistical analysis title | 20vPnC Versus 13vPnC |
|-----------------------------------|----------------------|

Statistical analysis description:

Serotype 8: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations.

| | |
|---|---|
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1129 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 26.55 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 22.98 |
| upper limit | 30.67 |

| | |
|---|---|
| Statistical analysis title | 20vPnC Versus 13vPnC |
| Statistical analysis description: Serotype 23F: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations. | |
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1129 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 0.52 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.44 |
| upper limit | 0.62 |

| | |
|---|---|
| Statistical analysis title | 20vPnC Versus 13vPnC |
| Statistical analysis description: Serotype 19F: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations. | |
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1129 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 0.72 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.64 |
| upper limit | 0.82 |

| | |
|---|---|
| Statistical analysis title | 20vPnC Versus 13vPnC |
| Statistical analysis description: Serotype 19A: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations. | |
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1129 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 0.59 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.51 |
| upper limit | 0.69 |

| | |
|-----------------------------------|----------------------|
| Statistical analysis title | 20vPnC Versus 13vPnC |
|-----------------------------------|----------------------|

Statistical analysis description:

Serotype 33F: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations.

| | |
|---|---|
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1129 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 5.03 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 4.27 |
| upper limit | 5.92 |

| | |
|-----------------------------------|----------------------|
| Statistical analysis title | 20vPnC Versus 13vPnC |
|-----------------------------------|----------------------|

Statistical analysis description:

Serotype 14: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations.

| | |
|---|---|
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1129 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 0.82 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.7 |
| upper limit | 0.96 |

| | |
|-----------------------------------|----------------------|
| Statistical analysis title | 20vPnC Versus 13vPnC |
|-----------------------------------|----------------------|

Statistical analysis description:

Serotype 18C: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations.

| | |
|-------------------|---|
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
|-------------------|---|

| | |
|---|----------------------|
| Number of subjects included in analysis | 1129 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 0.79 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.67 |
| upper limit | 0.92 |

Primary: GMC of Serotype-specific Pneumococcal IgG Antibody 1 Month After Dose 3: Primary Study Population

| | |
|-----------------|---|
| End point title | GMC of Serotype-specific Pneumococcal IgG Antibody 1 Month After Dose 3: Primary Study Population ^[23] |
|-----------------|---|

End point description:

Pneumococcal serotype-specific IgG concentrations were measured for serum samples for 13vPnC serotypes: 1,3,4, 5,6A,6B,7F,9V,14,18C,19A,19F, 23F, 7additional serotype: 8, 10A, 11A, 12F, 15B, 22F,33F. GMC & corresponding 2-sided 95% CI were calculated by exponentiating mean logarithm of concentrations & corresponding 2-sided 95% CI (based on Student's t distribution). Assay result below LLOQ were set to 0.5×LLOQ. GMRs were reported in statistical analysis section & were calculated by exponentiating mean difference of logarithm of concentration & corresponding 2-sided 95% CI (based on Student's t distribution). Dose 3 evaluable immunogenicity population (EIP) = eligible subject 42-112 days of age at first vaccination, received all 3 dose as randomized with 335-386 day of age at Dose 3 at least 1 valid immunogenicity results within 27-56 days after Dose 3, no major protocol deviation "Number of Subjects Analyzed" = subjects in Dose 3 EIP; "n" = subjects with valid IgG results for specified serotype.

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

End point timeframe:

1 month after Dose 3

Notes:

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

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

| End point values | 20vPnC: Primary Study Population | 13vPnC: Primary Study Population | | |
|--|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 497 | 504 | | |
| Units: mcg/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Serotype 1, n=494, 502 | 1.71 (1.58 to 1.84) | 2.53 (2.33 to 2.75) | | |
| Serotype 3, n=494, 502 | 0.72 (0.67 to 0.78) | 1.09 (1.01 to 1.17) | | |
| Serotype 4, n=494, 502 | 4.11 (3.77 to 4.48) | 5.36 (4.91 to 5.85) | | |
| Serotype 5, n=494, 502 | 1.74 (1.60 to 1.89) | 2.41 (2.21 to 2.64) | | |
| Serotype 6A, n=494, 501 | 7.75 (7.04 to 8.53) | 11.82 (10.66 to 13.11) | | |
| Serotype 6B, n=494, 501 | 2.64 (2.36 to 2.95) | 4.63 (4.09 to 5.25) | | |

| | | | | |
|--------------------------|------------------------|---------------------|--|--|
| Serotype 7F, n=494, 502 | 3.61 (3.40 to 3.84) | 4.93 (4.63 to 5.24) | | |
| Serotype 9V, n=494, 502 | 3.68 (3.42 to 3.97) | 5.04 (4.67 to 5.43) | | |
| Serotype 14, n=493, 501 | 4.52 (4.08 to 5.00) | 5.66 (5.12 to 6.26) | | |
| Serotype 18C, n=494, 502 | 2.71 (2.52 to 2.93) | 3.61 (3.33 to 3.91) | | |
| Serotype 19A, n=494, 502 | 4.51 (4.11 to 4.94) | 5.49 (5.02 to 6.01) | | |
| Serotype 19F, n=494, 502 | 6.19 (5.68 to 6.75) | 8.08 (7.40 to 8.83) | | |
| Serotype 23F, n=494, 502 | 2.64 (2.40 to 2.91) | 4.40 (3.95 to 4.90) | | |
| Serotype 8, n=495, 501 | 3.57 (3.32 to 3.83) | 0.03 (0.03 to 0.03) | | |
| Serotype 10A, n=495, 502 | 4.86 (4.41 to 5.36) | 0.01 (0.01 to 0.01) | | |
| Serotype 11A, n=495, 502 | 3.74 (3.44 to 4.07) | 0.02 (0.01 to 0.02) | | |
| Serotype 12F, n=495, 502 | 1.86 (1.71 to 2.01) | 0.01 (0.01 to 0.01) | | |
| Serotype 15B, n=495, 502 | 13.09 (12.10 to 14.15) | 0.02 (0.02 to 0.03) | | |
| Serotype 22F, n=495, 502 | 9.27 (8.52 to 10.08) | 0.00 (0.00 to 0.00) | | |
| Serotype 33F, n=495, 501 | 6.37 (5.83 to 6.95) | 0.01 (0.01 to 0.01) | | |

Statistical analyses

| Statistical analysis title | 20vPnC Versus 13vPnC |
|--|---|
| Statistical analysis description: | |
| Serotype 3: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations. | |
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1001 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 0.66 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.59 |
| upper limit | 0.73 |

| Statistical analysis title | 20vPnC Versus 13vPnC |
|--|----------------------|
| Statistical analysis description: | |
| Serotype 1: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations. | |

| | |
|---|---|
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1001 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 0.67 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.6 |
| upper limit | 0.75 |

| | |
|-----------------------------------|----------------------|
| Statistical analysis title | 20vPnC Versus 13vPnC |
|-----------------------------------|----------------------|

Statistical analysis description:

Serotype 4: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations.

| | |
|---|---|
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1001 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 0.77 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.68 |
| upper limit | 0.87 |

| | |
|-----------------------------------|----------------------|
| Statistical analysis title | 20vPnC Versus 13vPnC |
|-----------------------------------|----------------------|

Statistical analysis description:

Serotype 5: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations.

| | |
|---|---|
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1001 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 0.72 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.64 |
| upper limit | 0.81 |

| | |
|--|---|
| Statistical analysis title | 20vPnC Versus 13vPnC |
| Statistical analysis description: Serotype 6A: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations. | |
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1001 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 0.66 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.57 |
| upper limit | 0.75 |

| | |
|--|---|
| Statistical analysis title | 20vPnC Versus 13vPnC |
| Statistical analysis description: Serotype 6B: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations. | |
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1001 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 0.57 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.48 |
| upper limit | 0.67 |

| | |
|--|---|
| Statistical analysis title | 20vPnC Versus 13vPnC |
| Statistical analysis description: Serotype 7F: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations. | |
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |

| | |
|---|----------------------|
| Number of subjects included in analysis | 1001 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 0.73 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.67 |
| upper limit | 0.8 |

| | |
|-----------------------------------|----------------------|
| Statistical analysis title | 20vPnC Versus 13vPnC |
|-----------------------------------|----------------------|

Statistical analysis description:

Serotype 14: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations.

| | |
|---|---|
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1001 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 0.8 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.69 |
| upper limit | 0.92 |

| | |
|-----------------------------------|----------------------|
| Statistical analysis title | 20vPnC Versus 13vPnC |
|-----------------------------------|----------------------|

Statistical analysis description:

Serotype 9V: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations.

| | |
|---|---|
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1001 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 0.73 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.66 |
| upper limit | 0.81 |

| | |
|---|---|
| Statistical analysis title | 20vPnC Versus 13vPnC |
| Statistical analysis description: Serotype 18C: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations. | |
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1001 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 0.75 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.67 |
| upper limit | 0.84 |

| | |
|---|---|
| Statistical analysis title | 20vPnC Versus 13vPnC |
| Statistical analysis description: Serotype 12F: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations. | |
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1001 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 0.77 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.68 |
| upper limit | 0.87 |

| | |
|---|---|
| Statistical analysis title | 20vPnC Versus 13vPnC |
| Statistical analysis description: Serotype 11A: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations. | |
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1001 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 1.55 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.37 |
| upper limit | 1.75 |

| | |
|-----------------------------------|----------------------|
| Statistical analysis title | 20vPnC Versus 13vPnC |
|-----------------------------------|----------------------|

Statistical analysis description:

Serotype 19A: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations.

| | |
|---|---|
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1001 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 0.82 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.72 |
| upper limit | 0.93 |

| | |
|-----------------------------------|----------------------|
| Statistical analysis title | 20vPnC Versus 13vPnC |
|-----------------------------------|----------------------|

Statistical analysis description:

Serotype 19F: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations.

| | |
|---|---|
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1001 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 0.77 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.68 |
| upper limit | 0.87 |

| | |
|-----------------------------------|----------------------|
| Statistical analysis title | 20vPnC Versus 13vPnC |
|-----------------------------------|----------------------|

Statistical analysis description:

Serotype 23F: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations.

| | |
|-------------------|---|
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
|-------------------|---|

| | |
|---|----------------------|
| Number of subjects included in analysis | 1001 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 0.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.52 |
| upper limit | 0.69 |

| | |
|-----------------------------------|----------------------|
| Statistical analysis title | 20vPnC Versus 13vPnC |
|-----------------------------------|----------------------|

Statistical analysis description:

Serotype 8: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations.

| | |
|---|---|
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1001 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 1.48 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.32 |
| upper limit | 1.66 |

| | |
|-----------------------------------|----------------------|
| Statistical analysis title | 20vPnC Versus 13vPnC |
|-----------------------------------|----------------------|

Statistical analysis description:

Serotype 10A: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations.

| | |
|---|---|
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1001 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 2.02 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.77 |
| upper limit | 2.3 |

| | |
|---|---|
| Statistical analysis title | 20vPnC Versus 13vPnC |
| Statistical analysis description: Serotype 15B: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations. | |
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1001 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 5.42 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 4.82 |
| upper limit | 6.1 |

| | |
|---|---|
| Statistical analysis title | 20vPnC Versus 13vPnC |
| Statistical analysis description: Serotype 22F: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations. | |
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1001 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 3.84 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 3.4 |
| upper limit | 4.34 |

| | |
|---|---|
| Statistical analysis title | 20vPnC Versus 13vPnC |
| Statistical analysis description: Serotype 33F: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations. | |
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1001 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 2.64 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 2.33 |
| upper limit | 2.99 |

Primary: Percentage of Subjects With Predefined Antibody Levels for Concomitant Vaccine Antigens 1 Month After Dose 3: Primary Study Population

| | |
|-----------------|--|
| End point title | Percentage of Subjects With Predefined Antibody Levels for Concomitant Vaccine Antigens 1 Month After Dose 3: Primary Study Population ^[24] |
|-----------------|--|

End point description:

Diphtheria & tetanus toxoids:concentration(conc) of antibody(AB)(in international units[IU]) to diphtheria & tetanus toxoid(prespecified level \geq 0.1 IU/mL); Pertussis antigens-pertussis toxin (PT),filamentous hemagglutinin (FHA),pertactin (PRN):prespecified level \geq observed antipertussis AB concentration achieved by 95% of 13vPnC recipient; HBsAg prespecified level \geq 10 milli-IU per mL (mIU/mL); Poliovirus strains (types 1, 2, and 3): prespecified level: \geq 1:8; Haemophilus influenzae type b(Hib): prespecified level \geq 0.15 mcg/mL polyribosylribitol phosphate (anti-PRP) in mcg/mL.Dose3 EIP=eligible subject 42-112 day(D) of age at 1st vaccine,received 3 dose as randomized with 335-386 D of age at Dose3,1 valid immunogenicity result within 27-56 D after Dose3.n=subjects in Dose3 EIP.Concomitant vaccine response was assessed from subset of randomly selected study subjects.

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

End point timeframe:

1 month after Dose 3

Notes:

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

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

| End point values | 20vPnC: Primary Study Population | 13vPnC: Primary Study Population | | |
|----------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 497 | 504 | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Diphtheria toxoid, n=494, 498 | 99.6 (98.5 to 100.0) | 99.8 (98.9 to 100.0) | | |
| Tetanus toxoid, n=494, 498 | 99.4 (98.2 to 99.9) | 100.0 (99.3 to 100.0) | | |
| Pertussis: PT, n=494, 498 | 92.9 (90.3 to 95.0) | 95.2 (92.9 to 96.9) | | |
| Pertussis: FHA, n=494, 498 | 95.3 (93.1 to 97.0) | 95.2 (92.9 to 96.9) | | |
| Pertussis: PRN, n=494, 498 | 96.8 (94.8 to 98.1) | 95.2 (92.9 to 96.9) | | |
| Hepatitis B, n=173, 178 | 100.0 (97.9 to 100.0) | 98.9 (96.0 to 99.9) | | |
| Poliovirus: Type 1, n=81, 89 | 100.0 (95.5 to 100.0) | 100.0 (95.9 to 100.0) | | |
| Poliovirus: Type 2, n=81, 89 | 100.0 (95.5 to 100.0) | 100.0 (95.9 to 100.0) | | |
| Poliovirus: Type 3, n=81, 89 | 100.0 (95.5 to 100.0) | 100.0 (95.9 to 100.0) | | |

| | | | | |
|---|-----------------------|-----------------------|--|--|
| Haemophilus influenzae type b, n=185, 169 | 100.0 (98.0 to 100.0) | 100.0 (97.8 to 100.0) | | |
|---|-----------------------|-----------------------|--|--|

Statistical analyses

| | |
|---|---|
| Statistical analysis title | 20vPnC Versus 13vPnC |
| Statistical analysis description: PT: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage. | |
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1001 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Percent difference |
| Point estimate | -2.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -5.3 |
| upper limit | 0.7 |

| | |
|--|---|
| Statistical analysis title | 20vPnC Versus 13vPnC |
| Statistical analysis description: Tetanus: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions (20vPnC - 13vPnC) expressed as a percentage. | |
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1001 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Percent difference |
| Point estimate | -0.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.8 |
| upper limit | 0.2 |

| | |
|---|---|
| Statistical analysis title | 20vPnC Versus 13vPnC |
| Statistical analysis description: Diphtheria: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions (20vPnC - 13vPnC) expressed as a percentage. | |
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |

| | |
|---|--------------------|
| Number of subjects included in analysis | 1001 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Percent difference |
| Point estimate | -0.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.3 |
| upper limit | 0.8 |

| | |
|--|---|
| Statistical analysis title | 20vPnC Versus 13vPnC |
| Statistical analysis description: Poliovirus Type 1: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions (20vPnc - 13vPnC) expressed as a percentage. | |
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1001 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Percent difference |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -4.6 |
| upper limit | 4.2 |

| | |
|--|---|
| Statistical analysis title | 20vPnC Versus 13vPnC |
| Statistical analysis description: Poliovirus Type 2: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions (20vPnc - 13vPnC) expressed as a percentage. | |
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1001 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Percent difference |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -4.6 |
| upper limit | 4.2 |

| | |
|--|---|
| Statistical analysis title | 20vPnC Versus 13vPnC |
| Statistical analysis description: Poliovirus Type 3: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions (20vPnC - 13vPnC) expressed as a percentage. | |
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1001 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Percent difference |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -4.6 |
| upper limit | 4.2 |

| | |
|--|---|
| Statistical analysis title | 20vPnC Versus 13vPnC |
| Statistical analysis description: Hepatitis B: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions (20vPnC - 13vPnC) expressed as a percentage. | |
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1001 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Percent difference |
| Point estimate | 1.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.1 |
| upper limit | 4 |

| | |
|--|---|
| Statistical analysis title | 20vPnC Versus 13vPnC |
| Statistical analysis description: Hib: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions (20vPnC - 13vPnC) expressed as a percentage. | |
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1001 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Percent difference |
| Point estimate | 0 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2 |
| upper limit | 2.2 |

| | |
|-----------------------------------|----------------------|
| Statistical analysis title | 20vPnC Versus 13vPnC |
|-----------------------------------|----------------------|

Statistical analysis description:

FHA: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage.

| | |
|---|---|
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1001 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Percent difference |
| Point estimate | 0.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.6 |
| upper limit | 2.9 |

| | |
|-----------------------------------|----------------------|
| Statistical analysis title | 20vPnC Versus 13vPnC |
|-----------------------------------|----------------------|

Statistical analysis description:

PRN: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage.

| | |
|---|---|
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1001 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Percent difference |
| Point estimate | 1.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.9 |
| upper limit | 4.2 |

Primary: GMC of Measles Virus Antibody 1 Month After Dose 3: Primary Study Population

| | |
|-----------------|--|
| End point title | GMC of Measles Virus Antibody 1 Month After Dose 3: Primary Study Population ^[25] |
|-----------------|--|

End point description:

Pre-specified vaccine antigen (measles) was administered concomitantly with 20vPnC or 13vPnC at Dose 3 and responses measured 1 month after Dose 3. Assay results below the lower limit of quantitation (LLOQ) were set to 0.5*LLOQ in the analysis. GMCs and 2-sided 95% CIs were calculated by exponentiating the mean logarithm of the concentrations and the corresponding CIs (based on the Student's t distribution). The immune responses were only measured on random subset of subjects. Dose 3 evaluable immunogenicity population = eligible subjects 42-112 days of age at first vaccination, received all 3 doses as randomized with 335-386 days of age at Dose 3, at least 1 valid immunogenicity results from blood collection within 27 to 56 days after Dose 3, no major protocol deviations. Here, "Number of Subjects Analyzed"= subjects in Dose 3 evaluable immunogenicity population, received measles vaccine and had valid assay results measles vaccine antigen.

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

End point timeframe:

1 month after Dose 3

Notes:

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

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

| End point values | 20vPnC: Primary Study Population | 13vPnC: Primary Study Population | | |
|--|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 128 | 132 | | |
| Units: Arbitrary units per milliliter | | | | |
| geometric mean (confidence interval 95%) | 228.63 (186.34 to 280.52) | 216.72 (174.92 to 268.52) | | |

Statistical analyses

| | |
|----------------------------|----------------------|
| Statistical analysis title | 20vPnC Versus 13vPnC |
|----------------------------|----------------------|

Statistical analysis description:

Measles: GMR and 2-sided 95% CIs were calculated by exponentiating the mean differences of the logarithms of the concentrations (20vPnC – 13vPnC) and the corresponding CIs (based on the Student's t distribution).

| | |
|---|---|
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 260 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 1.05 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.79 |
| upper limit | 1.42 |

Primary: GMC of Rubella Virus Antibody 1 Month After Dose 3: Primary Study Population

| | |
|-----------------|--|
| End point title | GMC of Rubella Virus Antibody 1 Month After Dose 3: Primary Study Population ^[26] |
|-----------------|--|

End point description:

Pre-specified vaccine antigen (rubella) was administered concomitantly with 20vPnC or 13vPnC at Dose 3 and responses measured 1 month after Dose 3. Assay results below LLOQ were set to 0.5*LLOQ in the analysis. GMCs and 2-sided 95% CIs were calculated by exponentiating the mean logarithm of the concentrations and the corresponding CIs (based on the Student's t distribution). The immune responses were only measured on random subset of subjects. Dose 3 evaluable immunogenicity population = eligible subjects 42-112 days of age at first vaccination, received all 3 doses as randomized with 335-386 days of age at Dose 3, at least 1 valid immunogenicity results from blood collection within 27 to 56 days after Dose 3, no major protocol deviations. Here, "Number of Subjects Analyzed"= subjects in Dose 3 evaluable immunogenicity population, received rubella vaccine and had valid assay results rubella vaccine antigen.

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

End point timeframe:

1 month after Dose 3

Notes:

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

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

| End point values | 20vPnC: Primary Study Population | 13vPnC: Primary Study Population | | |
|---|----------------------------------|----------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 128 | 132 | | |
| Units: International units per milliliter | | | | |
| geometric mean (confidence interval 95%) | 31.81 (25.54 to 39.62) | 38.20 (32.10 to 45.45) | | |

Statistical analyses

| | |
|----------------------------|----------------------|
| Statistical analysis title | 20vPnC Versus 13vPnC |
|----------------------------|----------------------|

Statistical analysis description:

Rubella: GMR and 2-sided 95% CIs were calculated by exponentiating the mean differences of the logarithms of the concentrations (20vPnC – 13vPnC) and the corresponding CIs (based on the Student's t distribution).

| | |
|---|---|
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 260 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 0.83 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.63 |
| upper limit | 1.1 |

Primary: GMC of Mumps Virus Antibody 1 Month After Dose 3: Primary Study

Population

| | |
|-----------------|--|
| End point title | GMC of Mumps Virus Antibody 1 Month After Dose 3: Primary Study Population ^[27] |
|-----------------|--|

End point description:

Pre-specified vaccine antigen (mumps) was administered concomitantly with 20vPnC or 13vPnC at Dose 3 and responses measured 1 month after Dose 3. Assay results below the LLOQ were set to 0.5*LLOQ in the analysis. GMCs and 2-sided 95% CIs were calculated by exponentiating the mean logarithm of the concentrations and the corresponding CIs (based on the Student's t distribution). The immune responses were only measured on random subset of subjects. Dose 3 evaluable immunogenicity population = eligible subjects 42-112 days of age at first vaccination, received all 3 doses as randomized with 335-386 days of age at Dose 3, at least 1 valid immunogenicity results from blood collection within 27 to 56 days after Dose 3, no major protocol deviations. Here, "Number of Subjects Analyzed" = subjects in Dose 3 evaluable immunogenicity population, received mumps vaccine and had valid assay results mumps vaccine antigen.

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

End point timeframe:

1 month after Dose 3

Notes:

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

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

| End point values | 20vPnC: Primary Study Population | 13vPnC: Primary Study Population | | |
|--|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 128 | 133 | | |
| Units: Arbitrary units per milliliter | | | | |
| geometric mean (confidence interval 95%) | 36.81 (29.12 to 46.54) | 35.25 (28.14 to 44.17) | | |

Statistical analyses

| | |
|----------------------------|----------------------|
| Statistical analysis title | 20vPnC Versus 13vPnC |
|----------------------------|----------------------|

Statistical analysis description:

Mumps: GMR and 2-sided 95% CIs were calculated by exponentiating the mean differences of the logarithms of the concentrations (20vPnC – 13vPnC) and the corresponding CIs (based on the Student's t distribution).

| | |
|---|---|
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 261 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 1.04 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.76 |
| upper limit | 1.44 |

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

| | |
|-----------------|--|
| End point title | Percentage of Subjects With Local Reactions Within 7 Days After Dose 1: Russian Cohort ^[28] ^[29] |
|-----------------|--|

End point description:

Local reactions included redness, swelling and, pain at the injection site, recorded by parent's/legal guardians of subjects in an e-diary. Redness and swelling were measured and recorded in measuring device units. 1 measuring device unit = 0.5 cm. Redness and swelling were graded as mild (>0 to 2.0 cm), moderate (> 2.0 to 7.0 cm) and severe (>7.0 cm). Pain at injection site was graded as mild (hurt if gently touched example, whimpered, winced, protested, or withdrew), moderate (hurt if gently touched, with crying), and severe (caused limitation of limb movement). 95% CI was based on Clopper and Pearson method. Safety analysis set included all subjects who received at least 1 dose of 20vPnC or 13vPnC and had safety data assessed after any dose. Here, "Number of subjects Analyzed" signifies number of subjects with any e-diary data after Dose 1

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

End point timeframe:

Within 7 days after Dose 1

Notes:

[28] - 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: This endpoint was planned to be analysed only for the specified reporting arms

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

Justification: Only descriptive analysis was planned for this endpoint

| End point values | 20vPnC: Russian Cohort | 13vPnC: Russian Cohort | | |
|----------------------------------|---------------------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 24 | 27 | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Redness: Mild | 4.2 (0.1 to 21.1) | 7.4 (0.9 to 24.3) | | |
| Redness: Moderate | 4.2 (0.1 to 21.1) | 3.7 (0.1 to 19.0) | | |
| Redness: Severe | 0 (0.0 to 14.2) | 0 (0.0 to 12.8) | | |
| Swelling: Mild | 0 (0.0 to 14.2) | 0 (0.0 to 12.8) | | |
| Swelling: Moderate | 4.2 (0.1 to 21.1) | 0 (0.0 to 12.8) | | |
| Swelling: Severe | 0 (0.0 to 14.2) | 0 (0.0 to 12.8) | | |
| Pain at Injection Site: Mild | 8.3 (1.0 to 27.0) | 7.4 (0.9 to 24.3) | | |
| Pain at Injection Site: Moderate | 0 (0.0 to 14.2) | 3.7 (0.1 to 19.0) | | |
| Pain at Injection Site: Severe | 0 (0.0 to 14.2) | 0 (0.0 to 12.8) | | |

Statistical analyses

No statistical analyses for this end point

Primary: GMC of Varicella Virus Antibody 1 Month After Dose 3: Primary Study Population

| | |
|-----------------|--|
| End point title | GMC of Varicella Virus Antibody 1 Month After Dose 3: Primary Study Population ^[30] |
|-----------------|--|

End point description:

Pre-specified vaccine antigen (varicella) was administered concomitantly with 20vPnC or 13vPnC at Dose 3 and responses measured 1 month after Dose 3. Assay results below the lower limit of quantitation (LLOQ) were set to 0.5*LLOQ in the analysis. GMCs and 2-sided 95% CIs were calculated by exponentiating the mean logarithm of the concentrations and the corresponding CIs (based on the Student's t distribution). The immune responses were only measured on random subset of subjects. Dose 3 evaluable immunogenicity population = eligible subjects 42-112 days of age at first vaccination, received all 3 doses as randomized with 335-386 days of age at Dose 3, at least 1 valid immunogenicity results from blood collection within 27 to 56 days after Dose 3, no major protocol deviations. Here, "Number of Subjects Analyzed"= subjects in Dose 3 evaluable immunogenicity population, received varicella vaccine and had valid assay results varicella vaccine antigen.

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

End point timeframe:

1 month after Dose 3

Notes:

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

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

| End point values | 20vPnC: Primary Study Population | 13vPnC: Primary Study Population | | |
|---|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 128 | 132 | | |
| Units: Milli-international units per milliliter | | | | |
| geometric mean (confidence interval 95%) | 195.58 (165.14 to 231.62) | 157.60 (133.57 to 185.95) | | |

Statistical analyses

| | |
|----------------------------|----------------------|
| Statistical analysis title | 20vPnC Versus 13vPnC |
|----------------------------|----------------------|

Statistical analysis description:

Varicella: GMR and 2-sided 95% CIs were calculated by exponentiating the mean differences of the logarithms of the concentrations (20vPnC – 13vPnC) and the corresponding CIs (based on the Student's t distribution).

| | |
|---|---|
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 260 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Geometric Mean Ratio |
| Point estimate | 1.24 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.98 |
| upper limit | 1.57 |

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

Russian Cohort

| | |
|-----------------|--|
| End point title | Percentage of Subjects With Local Reactions Within 7 Days After Dose 2: Russian Cohort ^{[31][32]} |
|-----------------|--|

End point description:

Local reactions included redness, swelling and, pain at the injection site, recorded by parent's/legal guardians of subjects in an e-diary. Redness and swelling were measured and recorded in measuring device units. 1 measuring device unit = 0.5 cm. Redness and swelling were graded as mild (>0 to 2.0 cm), moderate (> 2.0 to 7.0 cm) and severe (>7.0 cm). Pain at injection site was graded as mild (hurt if gently touched example, whimpered, winced, protested, or withdrew), moderate (hurt if gently touched, with crying), and severe (caused limitation of limb movement). 95% CI was based on Clopper and Pearson method. Safety analysis set included all subjects who received at least 1 dose of 20vPnC or 13vPnC and had safety data assessed after any dose. Here, "Number of Subjects Analyzed" signifies the number of subjects with any e-diary data after Dose 2.

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

End point timeframe:

Within 7 days after Dose 2

Notes:

[31] - 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: This endpoint was planned to be analysed only for the specified reporting arms

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

Justification: Only descriptive analysis was planned for this endpoint

| End point values | 20vPnC: Russian Cohort | 13vPnC: Russian Cohort | | |
|----------------------------------|---------------------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 23 | 27 | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Redness: Mild | 0 (0.0 to 14.8) | 3.7 (0.1 to 19.0) | | |
| Redness: Moderate | 4.3 (0.1 to 21.9) | 0 (0.0 to 12.8) | | |
| Redness: Severe | 0 (0.0 to 14.8) | 0 (0.0 to 12.8) | | |
| Swelling: Mild | 0 (0.0 to 14.8) | 7.4 (0.9 to 24.3) | | |
| Swelling: Moderate | 8.7 (1.1 to 28.0) | 0 (0.0 to 12.8) | | |
| Swelling: Severe | 0 (0.0 to 14.8) | 0 (0.0 to 12.8) | | |
| Pain at Injection Site: Mild | 8.7 (1.1 to 28.0) | 7.4 (0.9 to 24.3) | | |
| Pain at Injection Site: Moderate | 4.3 (0.1 to 21.9) | 0 (0.0 to 12.8) | | |
| Pain at Injection Site: Severe | 0 (0.0 to 14.8) | 0 (0.0 to 12.8) | | |

Statistical analyses

No statistical analyses for this end point

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

| | |
|-----------------|--|
| End point title | Percentage of Subjects With Local Reactions Within 7 Days After Dose 3: Russian Cohort ^{[33][34]} |
|-----------------|--|

End point description:

Local reactions included redness, swelling and, pain at the injection site, recorded by parent's/legal guardians of subjects in an e-diary. Redness and swelling were measured and recorded in measuring device units. 1 measuring device unit =0.5 cm. Redness and swelling were graded as mild (>0 to 2.0 cm), moderate (> 2.0 to 7.0 cm) and severe (>7.0 cm). Pain at injection site was graded as mild (hurt if gently touched example, whimpered, winced, protested, or withdrew), moderate (hurt if gently touched, with crying), and severe (caused limitation of limb movement). 95% CI was based on Clopper and Pearson method. Safety analysis set included all subjects who received at least 1 dose of 20vPnC or 13vPnC and had safety data assessed after any dose. Here, "Number of Subjects Analyzed" signifies the number of subjects with any e-diary data after Dose 3.

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

End point timeframe:

Within 7 days after Dose 3

Notes:

[33] - 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: This endpoint was planned to be analysed only for the specified reporting arms

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

Justification: Only descriptive analysis was planned for this endpoint

| End point values | 20vPnC: Russian Cohort | 13vPnC: Russian Cohort | | |
|----------------------------------|---------------------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 22 | 25 | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Redness: Mild | 0 (0.0 to 15.4) | 4.0 (0.1 to 20.4) | | |
| Redness: Moderate | 4.5 (0.1 to 22.8) | 0 (0.0 to 13.7) | | |
| Redness: Severe | 0 (0.0 to 15.4) | 4.0 (0.1 to 4.0) | | |
| Swelling: Mild | 0 (0.0 to 15.4) | 0 (0.0 to 13.7) | | |
| Swelling: Moderate | 9.1 (1.1 to 29.2) | 0 (0.0 to 13.7) | | |
| Swelling: Severe | 0 (0.0 to 15.4) | 4.0 (0.1 to 20.4) | | |
| Pain at Injection Site: Mild | 13.6 (2.9 to 34.9) | 8.0 (1.0 to 26.0) | | |
| Pain at Injection Site: Moderate | 0 (0.0 to 15.4) | 0 (0.0 to 13.7) | | |
| Pain at Injection Site: Severe | 0 (0.0 to 15.4) | 0 (0.0 to 13.7) | | |

Statistical analyses

No statistical analyses for this end point

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

| | |
|-----------------|--|
| End point title | Percentage of Subjects With Systemic Events Within 7 Days After Dose 1: Russian cohort ^{[35][36]} |
|-----------------|--|

End point description:

Systemic events:fever,decreased appetite,drowsiness/increased sleep & irritability, recorded by parents/legal guardians of subject's using e-diary.Fever: temperature ≥ 38.0 degree C & categorized as ≥ 38.0 to 38.4 degree C, >38.4 to 38.9 degree C, >38.9 to 40.0 degree C & >40.0 -degree C. Decreased appetite:mild (decreased interest in eating), moderate (decreased oral intake) & severe (refusal to

feed).Drowsiness was graded as mild (increased/prolonged sleeping bouts), moderate (slightly subdued, interfered with daily activity) & severe (disabling, not interested in usual daily activity).Irritability: mild (easily consolable), moderate (required increased attention) & severe (inconsolable, crying could not be comforted).95% CI was based on Clopper & Pearson method. Safety analysis set:all subjects who received at least 1 dose of 20vPnC or 13vPnC & had safety data assessed after any dose.Here, "Number of subjects Analyzed" signifies number of subjects with any e-diary data after Dose 1.

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

End point timeframe:

Within 7 Days after Dose 1

Notes:

[35] - 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: This endpoint was planned to be analysed only for the specified reporting arms

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

Justification: Only descriptive analysis was planned for this endpoint

| End point values | 20vPnC: Russian Cohort | 13vPnC: Russian Cohort | | |
|---|---------------------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 24 | 27 | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Fever: >=38.0 degrees C to 38.4 degrees C | 4.2 (0.1 to 21.1) | 0 (0.0 to 12.8) | | |
| Fever: >38.4 degrees C to 38.9 degrees C | 0 (0.0 to 14.2) | 0 (0.0 to 12.8) | | |
| Fever: >38.9 degrees C to 40.0 degrees C | 0 (0.0 to 14.2) | 0 (0.0 to 12.8) | | |
| Fever: >40.0 degrees C | 0 (0.0 to 14.2) | 0 (0.0 to 12.8) | | |
| Decreased appetite: Mild | 16.7 (4.7 to 37.4) | 14.8 (4.2 to 33.7) | | |
| Decreased appetite: Moderate | 0 (0.0 to 14.2) | 3.7 (0.1 to 19.0) | | |
| Decreased appetite: Severe | 0 (0.0 to 14.2) | 0 (0.0 to 12.8) | | |
| Drowsiness: Mild | 20.8 (7.1 to 42.2) | 18.5 (6.3 to 38.1) | | |
| Drowsiness: Moderate | 8.3 (1.0 to 27.0) | 11.1 (2.4 to 29.2) | | |
| Drowsiness: Severe | 0 (0.0 to 14.2) | 0 (0.0 to 12.8) | | |
| Irritability: Mild | 12.5 (2.7 to 32.4) | 7.4 (0.9 to 24.3) | | |
| Irritability: Moderate | 8.3 (1.0 to 27.0) | 14.8 (4.2 to 33.7) | | |
| Irritability: Severe | 4.2 (0.1 to 21.1) | 0 (0.0 to 12.8) | | |

Statistical analyses

No statistical analyses for this end point

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

| | |
|-----------------|--|
| End point title | Percentage of Subjects With Systemic Events Within 7 Days After Dose 2: Russian cohort ^{[37][38]} |
|-----------------|--|

End point description:

Systemic events: fever, decreased appetite, drowsiness/increased sleep & irritability, recorded by parents/legal guardians of participant's using e-diary. Fever: temperature ≥ 38.0 degree C & categorized as ≥ 38.0 to 38.4 degree C, >38.4 to 38.9 degree C, >38.9 to 40.0 degree C & >40.0 -degree C. Decreased appetite: mild (decreased interest in eating), moderate (decreased oral intake) & severe (refusal to feed). Drowsiness was graded as mild (increased/prolonged sleeping bouts), moderate (slightly subdued, interfered with daily activity) & severe (disabling, not interested in usual daily activity). Irritability: mild (easily consolable), moderate (required increased attention) & severe (inconsolable, crying could not be comforted). 95% CI was based on Clopper & Pearson method. Safety analysis set: all subjects who received at least 1 dose of 20vPnC or 13vPnC & had safety data assessed after any dose. Here, "Number of Subjects Analyzed": number of subjects with any e-diary data after Dose 2

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

End point timeframe:

Within 7 Days after Dose 2

Notes:

[37] - 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: This endpoint was planned to be analysed only for the specified reporting arms

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

Justification: Only descriptive analysis was planned for this endpoint

| End point values | 20vPnC: Russian Cohort | 13vPnC: Russian Cohort | | |
|--|---------------------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 23 | 27 | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Fever: ≥ 38.0 degrees C to 38.4 degrees C | 0 (0.0 to 14.8) | 11.1 (2.4 to 29.2) | | |
| Fever: >38.4 degrees C to 38.9 degrees C | 4.3 (0.1 to 21.9) | 0 (0.0 to 12.8) | | |
| Fever: >38.9 degrees C to 40.0 degrees C | 0 (0.0 to 14.8) | 0 (0.0 to 12.8) | | |
| Fever: >40.0 degrees C | 0 (0.0 to 14.8) | 0 (0.0 to 12.8) | | |
| Decreased appetite: Mild | 4.3 (0.1 to 21.9) | 7.4 (0.9 to 24.3) | | |
| Decreased appetite: Moderate | 4.3 (0.1 to 21.9) | 3.7 (0.1 to 19.0) | | |
| Decreased appetite: Severe | 0 (0.0 to 14.8) | 0 (0.0 to 12.8) | | |
| Drowsiness: Mild | 4.3 (0.1 to 21.9) | 3.7 (0.1 to 19.0) | | |
| Drowsiness: Moderate | 0 (0.0 to 14.8) | 3.7 (0.1 to 19.0) | | |
| Drowsiness: Severe | 0 (0.0 to 14.8) | 0 (0.0 to 12.8) | | |
| Irritability: Mild | 13.0 (2.8 to 33.6) | 22.2 (8.6 to 42.3) | | |
| Irritability: Moderate | 4.3 (0.1 to 21.9) | 18.5 (6.3 to 38.1) | | |
| Irritability: Severe | 0 (0.0 to 14.8) | 3.7 (0.1 to 19.0) | | |

Statistical analyses

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

| | |
|-----------------|--|
| End point title | Percentage of Subjects With Systemic Events Within 7 Days After Dose 3: Russian cohort ^[39] ^[40] |
|-----------------|--|

End point description:

Systemic events: fever, decreased appetite, drowsiness/increased sleep & irritability, recorded by parents/legal guardians of subjects using e-diary. Fever: temperature ≥ 38.0 degree C & categorized as ≥ 38.0 to 38.4 degree C, >38.4 to 38.9 degree C, >38.9 to 40.0 degree C & >40.0 -degree C. Decreased appetite: mild (decreased interest in eating), moderate (decreased oral intake) & severe (refusal to feed). Drowsiness was graded as mild (increased/prolonged sleeping bouts), moderate (slightly subdued, interfered with daily activity) & severe (disabling, not interested in usual daily activity). Irritability: mild (easily consolable), moderate (required increased attention) & severe (inconsolable, crying could not be comforted). 95% CI was based on Clopper & Pearson method. Safety analysis set: all subjects who received at least 1 dose of 20vPnC or 13vPnC & had safety data assessed after any dose. Here, "Number of Subjects Analyzed": number of subjects with any e-diary data after Dose 3

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

End point timeframe:

Within 7 Days after Dose 3

Notes:

[39] - 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: This endpoint was planned to be analysed only for the specified reporting arms

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

Justification: Only descriptive analysis was planned for this endpoint

| End point values | 20vPnC: Russian Cohort | 13vPnC: Russian Cohort | | |
|--|---------------------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 22 | 25 | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Fever: ≥ 38.0 degrees C to 38.4 degrees C | 0 (0.0 to 15.4) | 0 (0.0 to 13.7) | | |
| Fever: >38.4 degrees C to 38.9 degrees C | 0 (0.0 to 15.4) | 4.0 (0.1 to 20.4) | | |
| Fever: >38.9 degrees C to 40.0 degrees C | 4.5 (0.1 to 22.8) | 0 (0.0 to 13.7) | | |
| Fever: >40.0 degrees C | 0 (0.0 to 15.4) | 0 (0.0 to 13.7) | | |
| Decreased appetite: Mild | 9.1 (1.1 to 29.2) | 8.0 (1.0 to 26.0) | | |
| Decreased appetite: Moderate | 9.1 (1.1 to 29.2) | 0 (0.0 to 13.7) | | |
| Decreased appetite: Severe | 0 (0.0 to 15.4) | 0 (0.0 to 13.7) | | |
| Drowsiness: Mild | 13.6 (2.9 to 34.9) | 20.0 (6.8 to 40.7) | | |
| Drowsiness: Moderate | 0 (0.0 to 15.4) | 4.0 (0.1 to 20.4) | | |
| Drowsiness: Severe | 0 (0.0 to 15.4) | 0 (0.0 to 13.7) | | |
| Irritability: Mild | 27.3 (10.7 to 50.2) | 16.0 (4.5 to 36.1) | | |
| Irritability: Moderate | 9.1 (1.1 to 29.2) | 8.0 (1.0 to 26.0) | | |
| Irritability: Severe | 0 (0.0 to 15.4) | 0 (0.0 to 13.7) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With SAEs From Dose 1 to 1 month after Dose 3: Russian cohort

| | |
|-----------------|--|
| End point title | Percentage of Subjects With SAEs From Dose 1 to 1 month after Dose 3: Russian cohort ^{[41][42]} |
|-----------------|--|

End point description:

An SAE was any untoward medical occurrence that occurred, at any dose: resulted in death; required inpatient hospitalization or prolongation of existing hospitalization; was life-threatening; resulted in persistent or significant disability/ incapacity; was a congenital anomaly/birth defect and other important medical events. 95% CI was based on the Clopper and Pearson method. Safety analysis set included all subjects who received at least 1 dose of 20vPnC or 13vPnC and had safety data assessed after any dose.

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

End point timeframe:

From Dose 1 to 1 month after Dose 3

Notes:

[41] - 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 analysis was planned for this endpoint

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

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

| End point values | 20vPnC: Russian Cohort | 13vPnC: Russian Cohort | | |
|----------------------------------|---------------------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 24 | 27 | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | 0 (0 to 0) | 0 (0 to 0) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With AEs From Dose 1 to 1 Month After Dose 2: Russian Cohort

| | |
|-----------------|---|
| End point title | Percentage of Subjects With AEs From Dose 1 to 1 Month After Dose 2: Russian Cohort ^{[43][44]} |
|-----------------|---|

End point description:

An AE was any untoward medical occurrence in a participant, temporally associated with the use of study treatment, whether or not considered related to the study treatment. 95% CI was based on the Clopper and Pearson method. Safety analysis set included all subjects who received at least 1 dose of 20vPnC or 13vPnC and had safety data assessed after any dose.

| | | | | |
|--|---------------------------|---------------------------|--|--|
| End point type | Primary | | | |
| End point timeframe: | | | | |
| From Dose 1 to 1 month after Dose 2 | | | | |
| Notes: | | | | |
| [43] - 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: This endpoint was planned to be analysed only for the specified reporting arms | | | | |
| [44] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. | | | | |
| Justification: Only descriptive analysis was planned for this endpoint | | | | |
| End point values | 20vPnC: Russian Cohort | 13vPnC: Russian Cohort | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 24 | 27 | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | 8.3 (1.0 to 27.0) | 3.7 (0.1 to 19.0) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With AEs From Dose 3 to 1 Month After Dose 3: Russian Cohort

| | | | | |
|---|---|---------------------------|--|--|
| End point title | Percentage of Subjects With AEs From Dose 3 to 1 Month After Dose 3: Russian Cohort ^[45] ^[46] | | | |
| End point description: | | | | |
| An AE was any untoward medical occurrence in a subject, temporally associated with the use of study treatment, whether or not considered related to the study treatment. 95% CI was based on the Clopper and Pearson method. AEs reported in this outcome measure excluded local reactions and systemic events. Safety analysis set included all subjects who received at least 1 dose of 20vPnC or 13vPnC and had safety data assessed after any dose. Here, "Number of Subjects Analyzed" signifies the number of subjects who received Dose 3. | | | | |
| End point type | Primary | | | |
| End point timeframe: | | | | |
| From Dose 3 to 1 month after Dose 3 | | | | |
| Notes: | | | | |
| [45] - 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 analysis was planned for this endpoint. | | | | |
| [46] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. | | | | |
| Justification: This endpoint was planned to be analysed only for the specified reporting arms | | | | |
| End point values | 20vPnC: Russian Cohort | 13vPnC: Russian Cohort | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 22 | 25 | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | 4.5 (0.1 to 22.8) | 0 (0.0 to 13.7) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Predefined Pneumococcal IgG Antibody 1 Month After Dose 2: Russian Cohort

| | |
|-----------------|---|
| End point title | Percentage of Subjects With Predefined Pneumococcal IgG Antibody 1 Month After Dose 2: Russian Cohort ^{[47][48]} |
|-----------------|---|

End point description:

Predefined IgG concentrations 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. 95% CI was based on the Clopper and Pearson method. Dose 2 evaluable immunogenicity population: eligible subjects 42-70 days of age at first vaccination, received first 2 doses as randomized, at least 1 valid immunogenicity results within 27 to 56 days after Dose 2, no other major protocol deviations. "Number of Subjects Analyzed"= subjects with valid IgG assay results for specified serotype.

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

End point timeframe:

1 month after Dose 2

Notes:

[47] - 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 analysis was planned for this endpoint

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

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

| End point values | 20vPnC: Russian Cohort | 13vPnC: Russian Cohort | | |
|----------------------------------|---------------------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 24 | 27 | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Serotype 1 | 70.8 (48.9 to 87.4) | 77.8 (57.7 to 91.4) | | |
| Serotype 3 | 37.5 (18.8 to 59.4) | 59.3 (38.8 to 77.6) | | |
| Serotype 4 | 75.0 (53.3 to 90.2) | 74.1 (53.7 to 88.9) | | |
| Serotype 5 | 66.7 (44.7 to 84.4) | 81.5 (61.9 to 93.7) | | |
| Serotype 6A | 54.2 (32.8 to 74.4) | 81.5 (61.9 to 93.7) | | |
| Serotype 6B | 20.8 (7.1 to 42.2) | 59.3 (38.8 to 77.6) | | |
| Serotype 7F | 95.8 (78.9 to 99.9) | 92.6 (75.7 to 99.1) | | |
| Serotype 9V | 41.7 (22.1 to 63.4) | 81.5 (61.9 to 93.7) | | |
| Serotype 14 | 83.3 (62.6 to 95.3) | 85.2 (66.3 to 95.8) | | |

| | | | | |
|--------------|---------------------|---------------------|--|--|
| Serotype 18C | 66.7 (44.7 to 84.4) | 81.5 (61.9 to 93.7) | | |
| Serotype 19A | 87.5 (67.6 to 97.3) | 92.6 (75.7 to 99.1) | | |
| Serotype 19F | 79.2 (57.8 to 92.9) | 96.3 (81.0 to 99.9) | | |
| Serotype 23F | 37.5 (18.8 to 59.4) | 70.4 (49.8 to 86.2) | | |
| Serotype 8 | 75.0 (53.3 to 90.2) | 33.3 (16.5 to 54.0) | | |
| Serotype 10A | 41.7 (22.1 to 63.4) | 18.5 (6.3 to 38.1) | | |
| Serotype 11A | 83.3 (62.6 to 95.3) | 18.5 (6.3 to 38.1) | | |
| Serotype 12F | 12.5 (2.7 to 32.4) | 14.8 (4.2 to 33.7) | | |
| Serotype 15B | 66.7 (44.7 to 84.4) | 33.3 (16.5 to 54.0) | | |
| Serotype 22F | 66.7 (44.7 to 84.4) | 14.8 (4.2 to 33.7) | | |
| Serotype 33F | 45.8 (25.6 to 67.2) | 25.9 (11.1 to 46.3) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With NDCMC From Dose 1 to 1 Month After Dose 3: Russian Cohort

| | |
|-----------------|---|
| End point title | Percentage of Subjects With NDCMC From Dose 1 to 1 Month After Dose 3: Russian Cohort ^{[49][50]} |
|-----------------|---|

End point description:

An NDCMC was defined as a disease or medical condition, not previously identified, that was expected to be persistent or was otherwise long-lasting in its effects. 95% CI was based on the Clopper and Pearson method. Safety analysis set included all subjects who received at least 1 dose of 20vPnC or 13vPnC and had safety data assessed after any dose.

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

End point timeframe:

From Dose 1 to 1 month after Dose 3

Notes:

[49] - 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 analysis was planned for this endpoint

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

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

| End point values | 20vPnC: Russian Cohort | 13vPnC: Russian Cohort | | |
|----------------------------------|---------------------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 24 | 27 | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | 0 (0 to 0) | 0 (0 to 0) | | |

Statistical analyses

No statistical analyses for this end point

Primary: GMC of Serotype-specific Pneumococcal IgG Antibody 1 Month After Dose 2: Russian Cohort

| | |
|-----------------|---|
| End point title | GMC of Serotype-specific Pneumococcal IgG Antibody 1 Month After Dose 2: Russian Cohort ^{[51][52]} |
|-----------------|---|

End point description:

Pneumococcal serotype-specific IgG concentrations were measured for serum samples for 13vPnC serotypes: 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F and 7 additional serotypes: 8, 10A, 11A, 12F, 15B, 22F, 33F. Assay results below the LLOQ were set to 0.5 × LLOQ. GMC & corresponding 2-sided 95% CIs were calculated by exponentiating mean logarithm of concentration, corresponding 2-sided 95% CIs (based on Student's t distribution). Dose 2 evaluable immunogenicity population: eligible subjects 42-70days of age at first vaccination, received first 2 doses as randomized, at least 1 valid immunogenicity results within 27 to 56 days after Dose 2, no other major protocol deviations. "Number of Subjects Analyzed"= subjects with valid IgG assay results for specified serotype.

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

End point timeframe:

1 month after Dose 2

Notes:

[51] - 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 analysis was planned for this endpoint

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

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

| End point values | 20vPnC: Russian Cohort | 13vPnC: Russian Cohort | | |
|--|---------------------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 24 | 27 | | |
| Units: mcg/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Serotype 1 | 0.76 (0.49 to 1.19) | 1.04 (0.64 to 1.69) | | |
| Serotype 3 | 0.28 (0.19 to 0.42) | 0.47 (0.31 to 0.72) | | |
| Serotype 4 | 0.67 (0.45 to 1.00) | 1.00 (0.58 to 1.71) | | |
| Serotype 5 | 0.53 (0.31 to 0.92) | 0.75 (0.40 to 1.40) | | |
| Serotype 6A | 0.45 (0.20 to 1.03) | 1.57 (0.80 to 3.10) | | |
| Serotype 6B | 0.07 (0.03 to 0.16) | 0.27 (0.12 to 0.63) | | |
| Serotype 7F | 1.06 (0.68 to 1.65) | 1.89 (1.32 to 2.71) | | |
| Serotype 9V | 0.44 (0.23 to 0.84) | 1.22 (0.73 to 2.06) | | |

| | | | | |
|--------------|---------------------|---------------------|--|--|
| Serotype 14 | 1.56 (0.88 to 2.75) | 2.66 (1.46 to 4.86) | | |
| Serotype 18C | 0.94 (0.46 to 1.91) | 0.94 (0.50 to 1.78) | | |
| Serotype 19A | 1.15 (0.47 to 2.82) | 1.21 (0.59 to 2.49) | | |
| Serotype 19F | 1.51 (0.84 to 2.72) | 3.32 (2.03 to 5.44) | | |
| Serotype 23F | 0.25 (0.11 to 0.55) | 0.73 (0.37 to 1.42) | | |
| Serotype 8 | 0.79 (0.37 to 1.69) | 0.07 (0.03 to 0.18) | | |
| Serotype 10A | 0.31 (0.10 to 0.94) | 0.04 (0.01 to 0.10) | | |
| Serotype 11A | 0.83 (0.43 to 1.60) | 0.04 (0.02 to 0.09) | | |
| Serotype 12F | 0.06 (0.03 to 0.11) | 0.02 (0.01 to 0.04) | | |
| Serotype 15B | 1.19 (0.46 to 3.05) | 0.16 (0.05 to 0.50) | | |
| Serotype 22F | 0.48 (0.16 to 1.47) | 0.02 (0.01 to 0.06) | | |
| Serotype 33F | 0.40 (0.18 to 0.88) | 0.07 (0.03 to 0.16) | | |

Statistical analyses

No statistical analyses for this end point

Primary: GMC of Serotype-specific Pneumococcal IgG Antibody 1 Month After Dose 3: Russian Cohort

| | |
|-----------------|---|
| End point title | GMC of Serotype-specific Pneumococcal IgG Antibody 1 Month After Dose 3: Russian Cohort ^[53] ^[54] |
|-----------------|---|

End point description:

Pneumococcal serotype-specific IgG concentrations were measured for serum samples for 13vPnC serotypes: 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F and additional serotypes: 8, 10A, 11A, 12F, 15B, 22F and 33F. Assay results below the LLOQ were set to 0.5 × LLOQ. GMC & corresponding 2-sided 95% CIs were calculated by exponentiating mean logarithm of concentration, corresponding 2-sided 95% CIs (based on Student's t distribution). Dose 3 evaluable immunogenicity population = eligible subjects 42-70 days of age at first vaccination, received all 3 doses as randomized with 335-455 days of age at Dose 3, at least 1 valid immunogenicity results from blood collection within 27 to 56 days after Dose 3, no major protocol deviations. Here, "Number of Subjects Analyzed" signifies the subjects with valid IgG assay result for specified serotype.

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

End point timeframe:

1 month after Dose 3

Notes:

[53] - 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 analysis was planned for this endpoint

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

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

| End point values | 20vPnC: Russian Cohort | 13vPnC: Russian Cohort | | |
|--|---------------------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 22 | 24 | | |
| Units: mcg/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Serotype 1 | 1.61 (0.93 to 2.78) | 1.65 (0.94 to 2.90) | | |
| Serotype 3 | 0.84 (0.44 to 1.60) | 0.57 (0.32 to 1.01) | | |
| Serotype 4 | 3.05 (1.50 to 6.20) | 3.04 (1.72 to 5.36) | | |
| Serotype 5 | 1.50 (0.80 to 2.82) | 1.72 (0.90 to 3.29) | | |
| Serotype 6A | 6.63 (2.96 to 14.86) | 5.63 (2.96 to 10.72) | | |
| Serotype 6B | 1.94 (0.82 to 4.56) | 1.49 (0.67 to 3.32) | | |
| Serotype 7F | 3.53 (1.97 to 6.33) | 4.14 (2.73 to 6.26) | | |
| Serotype 9V | 2.32 (1.28 to 4.19) | 2.27 (1.19 to 4.35) | | |
| Serotype 14 | 4.01 (1.64 to 9.77) | 5.06 (3.04 to 8.40) | | |
| Serotype 18C | 2.60 (1.24 to 5.44) | 2.64 (1.49 to 4.69) | | |
| Serotype 19A | 4.81 (2.07 to 11.16) | 2.69 (1.12 to 6.45) | | |
| Serotype 19F | 4.97 (2.30 to 10.76) | 4.58 (2.36 to 8.90) | | |
| Serotype 23F | 3.52 (1.68 to 7.38) | 2.96 (1.33 to 6.56) | | |
| Serotype 8 | 1.33 (0.50 to 3.56) | 0.09 (0.04 to 0.24) | | |
| Serotype 10A | 1.99 (0.63 to 6.29) | 0.03 (0.01 to 0.09) | | |
| Serotype 11A | 1.50 (0.58 to 3.87) | 0.06 (0.02 to 0.16) | | |
| Serotype 12F | 0.17 (0.05 to 0.56) | 0.02 (0.01 to 0.03) | | |
| Serotype 15B | 4.90 (1.67 to 14.37) | 0.07 (0.03 to 0.20) | | |
| Serotype 22F | 1.52 (0.38 to 6.03) | 0.02 (0.01 to 0.08) | | |
| Serotype 33F | 1.38 (0.53 to 3.59) | 0.04 (0.02 to 0.10) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Predefined Pneumococcal IgG Antibody 1 Month After Dose 3: Primary Study Population

| | |
|-----------------|---|
| End point title | Percentage of Subjects With Predefined Pneumococcal IgG Antibody 1 Month After Dose 3: Primary Study Population ^[55] |
|-----------------|---|

End point description:

Predefined IgG concentrations 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. 95% CI was based on the Clopper and Pearson method. Dose 3 evaluable immunogenicity population = eligible subjects 42-112 days of age at first vaccination, received all 3 doses as randomized with 335-386 days of age at Dose 3, at least 1 valid immunogenicity results from blood collection within 27 to 56 days after Dose 3, no major protocol deviations. "Number of Subjects Analyzed" = subjects in Dose 3 evaluable immunogenicity population; "n" = subjects with valid IgG results for specified serotype.

End point type Secondary

End point timeframe:

1 Month after Dose 3

Notes:

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

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

| End point values | 20vPnC: Primary Study Population | 13vPnC: Primary Study Population | | |
|----------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 497 | 504 | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Serotype 1, n=494, 502 | 97.2 (95.3 to 98.4) | 98.2 (96.6 to 99.2) | | |
| Serotype 3, n=494, 502 | 82.6 (79.0 to 85.8) | 93.2 (90.7 to 95.3) | | |
| Serotype 4, n=494, 502 | 99.2 (97.9 to 99.8) | 99.2 (98.0 to 99.8) | | |
| Serotype 5, n=494, 502 | 98.4 (96.8 to 99.3) | 98.0 (96.4 to 99.0) | | |
| Serotype 6A, n=494, 501 | 98.8 (97.4 to 99.6) | 98.8 (97.4 to 99.6) | | |
| Serotype 6B, n=494, 501 | 98.4 (96.8 to 99.3) | 97.6 (95.9 to 98.8) | | |
| Serotype 7F, n=494, 502 | 99.6 (98.5 to 100.0) | 100.0 (99.3 to 100.0) | | |
| Serotype 9V, n=494, 502 | 99.2 (97.9 to 99.8) | 98.8 (97.4 to 99.6) | | |
| Serotype 14, n=493, 501 | 96.6 (94.5 to 98.0) | 98.0 (96.4 to 99.0) | | |
| Serotype 18C, n=494, 502 | 99.2 (97.9 to 99.8) | 98.2 (96.6 to 99.2) | | |
| Serotype 19A, n=494, 502 | 99.6 (98.5 to 100.0) | 99.6 (98.6 to 100.0) | | |
| Serotype 19F, n=494, 502 | 99.6 (98.5 to 100.0) | 99.4 (98.3 to 99.9) | | |
| Serotype 23F, n=494, 502 | 96.4 (94.3 to 97.8) | 97.2 (95.4 to 98.5) | | |
| Serotype 8, n=495, 501 | 99.2 (97.9 to 99.8) | 3.6 (2.1 to 5.6) | | |
| Serotype 10A, n=495, 502 | 97.8 (96.1 to 98.9) | 1.6 (0.7 to 3.1) | | |
| Serotype 11A, n=495, 502 | 98.4 (96.8 to 99.3) | 4.6 (2.9 to 6.8) | | |
| Serotype 12F, n=495, 502 | 96.6 (94.6 to 98.0) | 0.2 (0.0 to 1.1) | | |
| Serotype 15B, n=495, 502 | 99.4 (98.2 to 99.9) | 4.8 (3.1 to 7.0) | | |

| | | | | |
|--------------------------|---------------------|------------------|--|--|
| Serotype 22F, n=495, 502 | 99.2 (97.9 to 99.8) | 1.4 (0.6 to 2.9) | | |
| Serotype 33F, n=495, 501 | 98.6 (97.1 to 99.4) | 1.8 (0.8 to 3.4) | | |

Statistical analyses

| Statistical analysis title | |
|--|---|
| 20vPnC Versus 13vPnC | |
| Statistical analysis description: | |
| Serotype 4: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage. | |
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1001 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Percent difference |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.4 |
| upper limit | 1.3 |

| Statistical analysis title | |
|--|---|
| 20vPnC Versus 13vPnC | |
| Statistical analysis description: | |
| Serotype 3: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage. | |
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1001 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Percent difference |
| Point estimate | -10.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -14.7 |
| upper limit | -6.7 |

| Statistical analysis title | |
|--|---|
| 20vPnC Versus 13vPnC | |
| Statistical analysis description: | |
| Serotype 1: 2-Sided 95% CIs are calculated using the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage. | |
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |

| | |
|---|--------------------|
| Number of subjects included in analysis | 1001 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Percent difference |
| Point estimate | -1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.1 |
| upper limit | 0.9 |

| | |
|---|---|
| Statistical analysis title | 20vPnC Versus 13vPnC |
| Statistical analysis description: Serotype 5: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage. | |
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1001 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Percent difference |
| Point estimate | 0.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.4 |
| upper limit | 2.2 |

| | |
|--|---|
| Statistical analysis title | 20vPnC Versus 13vPnC |
| Statistical analysis description: Serotype 6A: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage. | |
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1001 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Percent difference |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.6 |
| upper limit | 1.5 |

| | |
|--|---|
| Statistical analysis title | 20vPnC Versus 13vPnC |
| Statistical analysis description: Serotype 6B: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage. | |
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1001 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Percent difference |
| Point estimate | 0.8 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.1 |
| upper limit | 2.7 |

| | |
|--|---|
| Statistical analysis title | 20vPnC Versus 13vPnC |
| Statistical analysis description: Serotype 14: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage. | |
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1001 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Percent difference |
| Point estimate | -1.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.7 |
| upper limit | 0.6 |

| | |
|--|---|
| Statistical analysis title | 20vPnC Versus 13vPnC |
| Statistical analysis description: Serotype 9V: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage. | |
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1001 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Percent difference |
| Point estimate | 0.4 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1 |
| upper limit | 1.9 |

| | |
|-----------------------------------|----------------------|
| Statistical analysis title | 20vPnC Versus 13vPnC |
|-----------------------------------|----------------------|

Statistical analysis description:

Serotype 7F: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage.

| | |
|---|---|
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1001 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Percent difference |
| Point estimate | -0.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.5 |
| upper limit | 0.4 |

| | |
|-----------------------------------|----------------------|
| Statistical analysis title | 20vPnC Versus 13vPnC |
|-----------------------------------|----------------------|

Statistical analysis description:

Serotype 18C: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage.

| | |
|---|---|
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1001 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Percent difference |
| Point estimate | 1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.5 |
| upper limit | 2.7 |

| | |
|-----------------------------------|----------------------|
| Statistical analysis title | 20vPnC Versus 13vPnC |
|-----------------------------------|----------------------|

Statistical analysis description:

Serotype 19A: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage.

| | |
|-------------------|---|
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
|-------------------|---|

| | |
|---|--------------------|
| Number of subjects included in analysis | 1001 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Percent difference |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.1 |
| upper limit | 1.1 |

| | |
|---|---|
| Statistical analysis title | 20vPnC Versus 13vPnC |
| Statistical analysis description: Serotype 19F: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage. | |
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1001 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Percent difference |
| Point estimate | 0.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.9 |
| upper limit | 1.4 |

| | |
|---|---|
| Statistical analysis title | 20vPnC Versus 13vPnC |
| Statistical analysis description: Serotype 23F: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage. | |
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1001 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Percent difference |
| Point estimate | -0.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.2 |
| upper limit | 1.4 |

| | |
|---|---|
| Statistical analysis title | 20vPnC Versus 13vPnC |
| Statistical analysis description: Serotype 8: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage. | |
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1001 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Percent difference |
| Point estimate | 2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.4 |
| upper limit | 3.9 |

| | |
|---|---|
| Statistical analysis title | 20vPnC Versus 13vPnC |
| Statistical analysis description: Serotype 10A: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage. | |
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1001 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Percent difference |
| Point estimate | 0.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.5 |
| upper limit | 2.7 |

| | |
|---|---|
| Statistical analysis title | 20vPnC Versus 13vPnC |
| Statistical analysis description: Serotype 11A: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage. | |
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1001 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Percent difference |
| Point estimate | 1.2 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.7 |
| upper limit | 3.2 |

| | |
|-----------------------------------|----------------------|
| Statistical analysis title | 20vPnC Versus 13vPnC |
|-----------------------------------|----------------------|

Statistical analysis description:

Serotype 12F: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage.

| | |
|---|---|
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1001 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Percent difference |
| Point estimate | -0.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.9 |
| upper limit | 1.6 |

| | |
|-----------------------------------|----------------------|
| Statistical analysis title | 20vPnC Versus 13vPnC |
|-----------------------------------|----------------------|

Statistical analysis description:

Serotype 15B: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage.

| | |
|---|---|
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1001 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Percent difference |
| Point estimate | 2.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.7 |
| upper limit | 4.1 |

| | |
|-----------------------------------|----------------------|
| Statistical analysis title | 20vPnC Versus 13vPnC |
|-----------------------------------|----------------------|

Statistical analysis description:

Serotype 22F: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage.

| | |
|-------------------|---|
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
|-------------------|---|

| | |
|---|--------------------|
| Number of subjects included in analysis | 1001 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Percent difference |
| Point estimate | 2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.4 |
| upper limit | 3.9 |

| | |
|--|---|
| Statistical analysis title | 20vPnC Versus 13vPnC |
| Statistical analysis description: | |
| Serotype 33F: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage. | |
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1001 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Percent difference |
| Point estimate | 1.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.4 |
| upper limit | 3.4 |

Secondary: Geometric Mean Titers (GMTs) of Serotype-specific Opsonophagocytic Activity (OPA) 1 Month After Dose 2: Primary Study Population

| | |
|-----------------|--|
| End point title | Geometric Mean Titers (GMTs) of Serotype-specific Opsonophagocytic Activity (OPA) 1 Month After Dose 2: Primary Study Population ^[56] |
|-----------------|--|

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 randomly selected subsets of subjects at 1 month after Dose 2. Results were expressed as OPA titers. GMTs and 2-sided CIs were calculated by exponentiating the mean logarithm of the titers and the corresponding CIs based on the Student's t distribution. Dose 2 evaluable immunogenicity population: eligible subjects 42-112 days of age at first vaccination, received first 2 doses as randomized, at least 1 valid immunogenicity results within 27 to 56 days after Dose 2, no other major protocol deviations. "Number of Subjects Analyzed"= subjects in Dose 2 evaluable immunogenicity population, "n"= subjects with valid OPA assay results for specified serotype.

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

End point timeframe:

1 month after Dose 2

Notes:

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

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

| End point values | 20vPnC: Primary Study Population | 13vPnC: Primary Study Population | | |
|--|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 567 | 562 | | |
| Units: Titers | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Serotype 1, n=113, 107 | 14 (12 to 16) | 23 (19 to 28) | | |
| Serotype 3, n=114, 102 | 31 (26 to 36) | 40 (34 to 47) | | |
| Serotype 4, n=113, 112 | 333 (270 to 413) | 391 (314 to 486) | | |
| Serotype 5, n=112, 102 | 21 (18 to 23) | 27 (23 to 31) | | |
| Serotype 6A, n=112, 100 | 347 (273 to 441) | 409 (318 to 527) | | |
| Serotype 6B, n=106, 97 | 54 (42 to 71) | 105 (76 to 144) | | |
| Serotype 7F, n=114, 111 | 858 (736 to 1000) | 895 (781 to 1027) | | |
| Serotype 9V, n=567, 112 | 233 (182 to 298) | 285 (228 to 358) | | |
| Serotype 14, n=111, 101 | 287 (215 to 383) | 360 (264 to 489) | | |
| Serotype 18C, n=114, 112 | 588 (467 to 741) | 719 (590 to 876) | | |
| Serotype 19A, n=115, 111 | 57 (43 to 75) | 91 (69 to 121) | | |
| Serotype 19F, n=114, 103 | 97 (81 to 116) | 117 (94 to 146) | | |
| Serotype 23F, n=105, 108 | 59 (42 to 84) | 68 (48 to 96) | | |
| Serotype 8, n=103, 115 | 164 (133 to 203) | 17 (15 to 18) | | |
| Serotype 10A, n=109, 115 | 855 (610 to 1199) | 39 (34 to 44) | | |
| Serotype 11A, n=105, 116 | 327 (253 to 423) | 49 (47 to 51) | | |
| Serotype 12F, n=96, 116 | 4788 (3779 to 6067) | 26 (23 to 28) | | |
| Serotype 15B, n=104, 117 | 846 (605 to 1183) | 17 (15 to 19) | | |
| Serotype 22F, n=104, 117 | 4444 (3666 to 5386) | 10 (9 to 11) | | |
| Serotype 33F, n=102, 115 | 2373 (1759 to 3202) | 178 (163 to 195) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titers (GMTs) of Serotype-specific Opsonophagocytic Activity (OPA) 1 Month After Dose 3: Primary Study Population

| | |
|-----------------|--|
| End point title | Geometric Mean Titers (GMTs) of Serotype-specific Opsonophagocytic Activity (OPA) 1 Month After Dose 3: Primary Study Population ^[57] |
|-----------------|--|

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 randomly selected subsets of subjects 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 titers and the corresponding CIs based on the Student's t distribution. Dose 3 evaluable immunogenicity population = eligible subjects 42-112 days of age at first vaccination, received all 3 doses as randomized with 335-386 days of age at Dose 3, at least 1 valid immunogenicity results from blood collection within 27 to 56 days after Dose 3, no major protocol deviations. "Number of Subjects Analyzed"= subjects in Dose 3 evaluable immunogenicity population; "n"= subjects with valid assay results for specified OPA serotype.

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

End point timeframe:

1 Month after Dose 3

Notes:

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

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

| End point values | 20vPnC: Primary Study Population | 13vPnC: Primary Study Population | | |
|--|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 497 | 504 | | |
| Units: Titers | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Serotype 1, n=104, 97 | 54 (43 to 69) | 101 (79 to 129) | | |
| Serotype 3, n=105, 98 | 99 (84 to 117) | 129 (111 to 150) | | |
| Serotype 4, n=99, 100 | 904 (752 to 1086) | 992 (777 to 1266) | | |
| Serotype 5, n=106, 98 | 60 (50 to 72) | 82 (66 to 101) | | |
| Serotype 6A, n=105, 96 | 1101 (897 to 1350) | 1304 (1018 to 1671) | | |
| Serotype 6B, n=102, 96 | 537 (408 to 706) | 864 (664 to 1125) | | |
| Serotype 7F, n=100, 103 | 1811 (1553 to 2112) | 2197 (1905 to 2533) | | |
| Serotype 9V, n=97, 99 | 3254 (2596 to 4079) | 4544 (3681 to 5610) | | |
| Serotype 14, n=105, 95 | 738 (606 to 899) | 926 (751 to 1142) | | |
| Serotype 18C, n=98, 102 | 1296 (1048 to 1602) | 1870 (1489 to 2348) | | |
| Serotype 19A, n=99, 100 | 754 (627 to 907) | 707 (558 to 896) | | |
| Serotype 19F, n=105, 97 | 183 (140 to 237) | 258 (192 to 347) | | |
| Serotype 23F, n=100, 101 | 697 (530 to 917) | 975 (734 to 1296) | | |
| Serotype 8, n=92, 105 | 1398 (1088 to 1796) | 31 (25 to 39) | | |
| Serotype 10A, n=91, 107 | 3403 (2600 to 4455) | 69 (52 to 91) | | |
| Serotype 11A, n=87, 92 | 2966 (2212 to 3978) | 66 (51 to 85) | | |
| Serotype 12F, n=88, 108 | 5501 (4499 to 6725) | 29 (25 to 35) | | |
| Serotype 15B, n=91, 504 | 2676 (1948 to 3677) | 23 (18 to 30) | | |
| Serotype 22F, n=83, 103 | 6523 (4848 to 8777) | 17 (13 to 24) | | |

| | | | | |
|------------------------|-----------------------|------------------|--|--|
| Serotype 33F, n=72, 99 | 11315 (8107 to 15794) | 708 (545 to 920) | | |
|------------------------|-----------------------|------------------|--|--|

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Fold Rise (GMFRs) of IgG Concentrations From Before Dose 3 to 1 Month After Dose 3: Primary Study Population

| | |
|-----------------|---|
| End point title | Geometric Mean Fold Rise (GMFRs) of IgG Concentrations From Before Dose 3 to 1 Month After Dose 3: Primary Study Population ^[58] |
|-----------------|---|

End point description:

20vPnC serotypes included: 1, 3, 4, 5, 6A, 6B, 7F, 8, 9V, 10A, 11A, 12F, 14, 15B, 18C, 19A, 19F, 22F, 23F, and 33F. Assay results below the LLOQ were set to 0.5*LLOQ in the analysis. GMFRs and the corresponding 2-sided CIs were calculated by exponentiating the mean logarithm of the fold rises and the corresponding CIs (based on the Student's t distribution). Dose 3 evaluable immunogenicity population = eligible subjects 42-112 days of age at first vaccination, received all 3 doses as randomized with 335-386 days of age at Dose 3, at least 1 valid immunogenicity results from blood collection within 27 to 56 days after Dose 3, no major protocol deviations. "Number of Subjects Analyzed"= subjects in Dose 3 evaluable immunogenicity population; "n"= subjects with valid IgG assay results for specified serotype at both timepoints

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

End point timeframe:

1 month after Dose 3

Notes:

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

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

| End point values | 20vPnC: Primary Study Population | 13vPnC: Primary Study Population | | |
|--|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 497 | 504 | | |
| Units: Fold rise | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Serotype 1, n=482, 495 | 13.9 (12.7 to 15.3) | 13.9 (12.8 to 15.1) | | |
| Serotype 3, n=482, 495 | 13.7 (12.4 to 15.1) | 15.2 (13.9 to 16.7) | | |
| Serotype 4, n=482, 495 | 29.8 (27.0 to 32.9) | 27.7 (25.0 to 30.6) | | |
| Serotype 5, n=482, 495 | 14.0 (12.9 to 15.2) | 13.6 (12.6 to 14.7) | | |
| Serotype 6A, n=482, 493 | 26.9 (24.2 to 30.0) | 28.7 (25.9 to 31.7) | | |
| Serotype 6B, n=481, 493 | 36.8 (33.3 to 40.6) | 40.2 (36.8 to 44.0) | | |
| Serotype 7F, n=482, 495 | 8.5 (7.9 to 9.2) | 9.3 (8.6 to 10.0) | | |
| Serotype 9V, n=482, 495 | 22.5 (20.4 to 24.7) | 19.9 (18.3 to 21.6) | | |

| | | | | |
|--------------------------|---------------------|---------------------|--|--|
| Serotype 14, n=480, 494 | 9.7 (8.7 to 10.8) | 8.4 (7.6 to 9.4) | | |
| Serotype 18C, n=482, 495 | 15.8 (14.5 to 17.1) | 17.0 (15.7 to 18.4) | | |
| Serotype 19A, n=481, 495 | 39.3 (34.6 to 44.7) | 40.7 (36.4 to 45.5) | | |
| Serotype 19F, n=482, 495 | 20.5 (18.4 to 22.9) | 21.4 (19.4 to 23.7) | | |
| Serotype 23F, n=482, 495 | 32.3 (29.2 to 35.7) | 38.3 (34.7 to 42.4) | | |
| Serotype 8, n=483, 493 | 12.7 (11.6 to 13.9) | 1.4 (1.3 to 1.5) | | |
| Serotype 10A, n=484, 495 | 14.8 (13.3 to 16.4) | 1.1 (1.0 to 1.2) | | |
| Serotype 11A, n=484, 495 | 13.8 (12.4 to 15.3) | 1.1 (1.0 to 1.2) | | |
| Serotype 12F, n=484, 495 | 16.5 (15.0 to 18.0) | 1.0 (1.0 to 1.1) | | |
| Serotype 15B, n=484, 495 | 13.4 (11.9 to 15.1) | 1.3 (1.2 to 1.4) | | |
| Serotype 22F, n=484, 495 | 12.8 (11.5 to 14.3) | 1.3 (1.1 to 1.4) | | |
| Serotype 33F, n=484, 494 | 12.9 (11.6 to 14.3) | 1.1 (1.0 to 1.2) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Predefined Antibody Levels for Concomitant Vaccine Antigens 1 Month After Dose 2: Primary Study Population

| | |
|-----------------|--|
| End point title | Percentage of Subjects With Predefined Antibody Levels for Concomitant Vaccine Antigens 1 Month After Dose 2: Primary Study Population ^[59] |
|-----------------|--|

End point description:

Diphtheria & tetanus toxoids:concentration(conc) of antibody(AB)(in international units[IU]) to diphtheria & tetanus toxoid(prespecified level \geq 0.1 IU/mL); Pertussis antigens-pertussis toxin (PT),filamentous hemagglutinin (FHA),pertactin (PRN):prespecified level \geq observed antipertussis AB concentration achieved by 95% of 13vPnC recipient; HBsAg prespecified level \geq 10 milli-IU per mL (mIU/mL); Poliovirus strains (types 1, 2, and 3): prespecified level: \geq 1:8; Haemophilus influenzae type b(Hib): prespecified level \geq 0.15 mcg/mL polyribosylribitol phosphate (anti-PRP) in mcg/mL.Dose3 EIP=eligible subject 42-112 day(D) of age at 1st vaccine,received 2 dose as randomized,1 valid immunogenicity result within 27-56 D after Dose2."Number of Subjects Analyzed"=subjects in Dose 3 evaluable immunogenicity population; Concomitant vaccine response was assessed from subset of randomly selected study subjects.

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

End point timeframe:

1 month after Dose 2

Notes:

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

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

| End point values | 20vPnC: Primary Study Population | 13vPnC: Primary Study Population | | |
|---|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 567 | 562 | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Diphtheria toxoid, n=170, 179 | 85.0 (79.3 to 89.6) | 89.5 (84.4 to 93.4) | | |
| Tetanus toxoid, n=191, 197 | 95.5 (91.6 to 97.9) | 98.5 (95.7 to 99.7) | | |
| Pertussis: PT, n=189, 190 | 94.5 (90.4 to 97.2) | 95.0 (91.0 to 97.6) | | |
| Pertussis: FHA, n=187, 190 | 93.5 (89.1 to 96.5) | 95.0 (91.0 to 97.6) | | |
| Pertussis: PRN, n=187, 190 | 93.5 (89.1 to 96.5) | 95.0 (91.0 to 97.6) | | |
| Poliovirus: Type 1, n=91, 102 | 94.8 (88.3 to 98.3) | 98.1 (93.2 to 99.8) | | |
| Poliovirus: Type 2, n=85, 95 | 88.5 (80.4 to 94.1) | 91.3 (84.2 to 96.0) | | |
| Poliovirus: Type 3, n=92, 104 | 95.8 (89.7 to 98.9) | 100.0 (96.5 to 100.0) | | |
| Haemophilus influenzae type b, n=207, 193 | 100.0 (98.2 to 100.0) | 100.0 (98.1 to 100.0) | | |

Statistical analyses

| Statistical analysis title | 20vPnC Versus 13vPnC |
|--|---|
| Statistical analysis description: | |
| Diphtheria: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions (20vPnC - 13vPnC) expressed as a percentage. | |
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1129 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Percent difference |
| Point estimate | -4.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -11.2 |
| upper limit | 2.1 |

| Statistical analysis title | 20vPnC Versus 13vPnC |
|---|---|
| Statistical analysis description: | |
| Tetanus: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions (20vPnC - 13vPnC) expressed as a percentage. | |
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |

| | |
|---|--------------------|
| Number of subjects included in analysis | 1129 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Percent difference |
| Point estimate | -3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -7 |
| upper limit | 0.4 |

| | |
|-----------------------------------|----------------------|
| Statistical analysis title | 20vPnC Versus 13vPnC |
|-----------------------------------|----------------------|

Statistical analysis description:

PT: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions (20vPnC - 13vPnC) expressed as a percentage.

| | |
|---|---|
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1129 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Percent difference |
| Point estimate | -0.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -5.2 |
| upper limit | 4.1 |

| | |
|-----------------------------------|----------------------|
| Statistical analysis title | 20vPnC Versus 13vPnC |
|-----------------------------------|----------------------|

Statistical analysis description:

FHA: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions (20vPnC - 13vPnC) expressed as a percentage.

| | |
|---|---|
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1129 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Percent difference |
| Point estimate | -1.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -6.4 |
| upper limit | 3.3 |

| | |
|--|---|
| Statistical analysis title | 20vPnC Versus 13vPnC |
| Statistical analysis description: PRN: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions (20vPnC - 13vPnC) expressed as a percentage. | |
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1129 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Percent difference |
| Point estimate | -1.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -6.4 |
| upper limit | 3.3 |

| | |
|--|---|
| Statistical analysis title | 20vPnC Versus 13vPnC |
| Statistical analysis description: Poliovirus Type 1: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions (20vPnC - 13vPnC) expressed as a percentage. | |
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1129 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Percent difference |
| Point estimate | -3.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -10 |
| upper limit | 2.2 |

| | |
|--|---|
| Statistical analysis title | 20vPnC Versus 13vPnC |
| Statistical analysis description: Poliovirus Type 2: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions (20vPnC - 13vPnC) expressed as a percentage. | |
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1129 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Percent difference |
| Point estimate | -2.8 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -11.8 |
| upper limit | 5.8 |

| | |
|-----------------------------------|----------------------|
| Statistical analysis title | 20vPnC Versus 13vPnC |
|-----------------------------------|----------------------|

Statistical analysis description:

Poliovirus Type 3: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions (20vPnC - 13vPnC) expressed as a percentage.

| | |
|---|---|
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1129 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Percent difference |
| Point estimate | -4.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -10.2 |
| upper limit | -0.5 |

| | |
|-----------------------------------|----------------------|
| Statistical analysis title | 20vPnC Versus 13vPnC |
|-----------------------------------|----------------------|

Statistical analysis description:

Hib: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions (20vPnC - 13vPnC) expressed as a percentage.

| | |
|---|---|
| Comparison groups | 20vPnC: Primary Study Population v 13vPnC: Primary Study Population |
| Number of subjects included in analysis | 1129 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Percent difference |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.8 |
| upper limit | 2 |

Secondary: Percentage of Subjects With Predefined Pneumococcal IgG Antibody 1 Month After Dose 3: Russian Cohort

| | |
|-----------------|---|
| End point title | Percentage of Subjects With Predefined Pneumococcal IgG Antibody 1 Month After Dose 3: Russian Cohort ^[60] |
|-----------------|---|

End point description:

Predefined IgG concentrations 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. 95% CI was based on the Clopper and Pearson method. Dose 3 evaluable immunogenicity population = eligible subjects 42-70 days of age at first vaccination, received all 3 doses as randomized with 335-455 days of age at Dose 3, at least 1 valid immunogenicity results from blood collection within 27 to 56 days after Dose 3, no major protocol deviations. "Number of Subjects Analyzed"= subjects in Dose 3 evaluable immunogenicity population.

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

End point timeframe:

1 Month after Dose 3

Notes:

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

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

| End point values | 20vPnC: Russian Cohort | 13vPnC: Russian Cohort | | |
|----------------------------------|---------------------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 22 | 24 | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Serotype 1 | 90.9 (70.8 to 98.9) | 83.3 (62.6 to 95.3) | | |
| Serotype 3 | 68.2 (45.1 to 86.1) | 50.0 (29.1 to 70.9) | | |
| Serotype 4 | 95.5 (77.2 to 99.9) | 100.0 (85.8 to 100.0) | | |
| Serotype 5 | 90.9 (70.8 to 98.9) | 91.7 (73.0 to 99.0) | | |
| Serotype 6A | 95.5 (77.2 to 99.9) | 100.0 (85.8 to 100.0) | | |
| Serotype 6B | 90.9 (70.8 to 98.9) | 91.7 (73.0 to 99.0) | | |
| Serotype 7F | 95.5 (77.2 to 99.0) | 100.0 (85.8 to 100.0) | | |
| Serotype 9V | 100.0 (84.6 to 100.0) | 83.3 (62.6 to 95.3) | | |
| Serotype 14 | 90.9 (70.8 to 98.9) | 100.0 (85.8 to 100.0) | | |
| Serotype 18C | 90.9 (70.8 to 98.9) | 95.8 (78.9 to 99.9) | | |
| Serotype 19A | 100.0 (84.6 to 100.0) | 95.8 (78.9 to 99.9) | | |
| Serotype 19F | 100.0 (84.6 to 100.0) | 91.7 (73.0 to 99.0) | | |
| Serotype 23F | 90.9 (70.8 to 98.9) | 79.2 (57.8 to 92.9) | | |
| Serotype 8 | 68.2 (45.1 to 86.1) | 25.0 (9.8 to 46.7) | | |
| Serotype 10A | 68.2 (45.1 to 86.1) | 16.7 (4.7 to 37.4) | | |
| Serotype 11A | 77.3 (54.6 to 92.2) | 20.8 (7.1 to 42.2) | | |
| Serotype 12F | 36.4 (17.2 to 59.3) | 4.2 (0.1 to 21.1) | | |
| Serotype 15B | 90.9 (70.8 to 98.9) | 20.8 (7.1 to 42.2) | | |

| | | | | |
|--------------|---------------------|--------------------|--|--|
| Serotype 22F | 63.6 (40.7 to 82.8) | 12.5 (2.7 to 32.4) | | |
| Serotype 33F | 72.7 (49.8 to 89.3) | 20.8 (7.1 to 42.2) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: GMTs of Serotype-specific OPA 1 Month After Dose 2: Russian Cohort

| | |
|-----------------|--|
| End point title | GMTs of Serotype-specific OPA 1 Month After Dose 2: Russian Cohort ^[61] |
|-----------------|--|

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 randomly selected subsets of subjects at 1 month after Dose 2. Results were expressed as OPA titers. GMTs and 2-sided CIs were calculated by exponentiating the mean logarithm of the titers and the corresponding CIs based on the Student's t distribution. Dose 2 evaluable immunogenicity population: eligible subjects 42-70 days of age at first vaccination, received first 2 doses as randomized, at least 1 valid immunogenicity results from blood collection (27 to 56 days after Dose 2), no other major protocol deviations. "Number of Subjects Analyzed"= subjects in Dose 2 evaluable immunogenicity population, "n"= subjects with valid OPA assay results for specified serotype.

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

End point timeframe:

1 month after Dose 2

Notes:

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

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

| End point values | 20vPnC: Russian Cohort | 13vPnC: Russian Cohort | | |
|--|---------------------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 24 | 27 | | |
| Units: Titers | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Serotype 1, n=8, 9 | 17 (7 to 40) | 33 (10 to 105) | | |
| Serotype 3, n=8, 9 | 79 (42 to 149) | 31 (13 to 73) | | |
| Serotype 4, n=8, 9 | 166 (38 to 736) | 163 (32 to 840) | | |
| Serotype 5, n=8, 9 | 28 (11 to 76) | 31 (14 to 71) | | |
| Serotype 6A, n=8, 9 | 222 (32 to 1553) | 247 (60 to 1011) | | |
| Serotype 6B, n=7, 8 | 314 (27 to 3584) | 216 (39 to 1186) | | |
| Serotype 7F, n=8, 9 | 809 (481 to 1361) | 717 (246 to 2084) | | |
| Serotype 9V, n=8, 9 | 218 (70 to 676) | 293 (85 to 1008) | | |
| Serotype 14, n=7, 9 | 984 (492 to 1970) | 247 (69 to 886) | | |
| Serotype 18C, n=8, 9 | 968 (403 to 2326) | 268 (43 to 1655) | | |

| | | | | |
|----------------------|---------------------|---------------------|--|--|
| Serotype 19A, n=7, 9 | 314 (68 to 1443) | 31 (8 to 118) | | |
| Serotype 19F, n=8, 9 | 120 (27 to 529) | 230 (48 to 1097) | | |
| Serotype 23F, n=8, 9 | 35 (6 to 196) | 56 (9 to 346) | | |
| Serotype 8, n=7, 9 | 203 (19 to 2155) | 38 (9 to 161) | | |
| Serotype 10A, n=6, 5 | 559 (50 to 6233) | 232 (8 to 6478) | | |
| Serotype 11A, n=6, 7 | 3537 (863 to 14497) | 2717 (470 to 15716) | | |
| Serotype 12F, n=7, 9 | 698 (77 to 6301) | 198 (41 to 960) | | |
| Serotype 15B, n=7, 8 | 142 (9 to 2269) | 242 (18 to 3267) | | |
| Serotype 22F, n=7, 8 | 413 (32 to 5406) | 499 (28 to 8837) | | |
| Serotype 33F, n=7, 9 | 3508 (349 to 35250) | 3961 (706 to 22238) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: GMTs of Serotype-specific OPA 1 Month After Dose 3: Russian Cohort

| | |
|-----------------|--|
| End point title | GMTs of Serotype-specific OPA 1 Month After Dose 3: Russian Cohort ^[62] |
|-----------------|--|

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 randomly selected subsets of subjects 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 titers and the corresponding CIs based on the Student's t distribution. Dose 3 evaluable immunogenicity population = eligible subjects 42-70 days of age at first vaccination, received all 3 doses as randomized with 335-455 days of age at Dose 3, at least 1 valid immunogenicity results from blood collection within 27 to 56 days after Dose 3, no major protocol deviations. "Number of Subjects Analyzed"= subjects in Dose 3 evaluable immunogenicity population; "n"= subjects with valid OPA assay results for specified serotype.

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

End point timeframe:

1 Month after Dose 3

Notes:

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

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

| End point values | 20vPnC: Russian Cohort | 13vPnC: Russian Cohort | | |
|--|---------------------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 22 | 24 | | |
| Units: Titers | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Serotype 1, n=8, 9 | 85 (17 to 421) | 93 (22 to 394) | | |
| Serotype 3, n=8, 9 | 126 (41 to 383) | 107 (37 to 309) | | |

| | | | | |
|----------------------|----------------------|---------------------|--|--|
| Serotype 4, n=8, 8 | 310 (86 to 1123) | 429 (38 to 4863) | | |
| Serotype 5, n=8, 9 | 116 (28 to 476) | 108 (26 to 456) | | |
| Serotype 6A, n=7, 9 | 2922 (311 to 27459) | 1580 (393 to 6351) | | |
| Serotype 6B, n=7, 7 | 4417 (998 to 19951) | 1397 (150 to 12967) | | |
| Serotype 7F, n=8, 8 | 1039 (509 to 2122) | 1411 (373 to 5340) | | |
| Serotype 9V, n=8, 7 | 1574 (369 to 6711) | 1067 (150 to 7583) | | |
| Serotype 14, n=7, 9 | 1151 (321 to 4132) | 628 (137 to 2890) | | |
| Serotype 18C, n=8, 8 | 583 (149 to 2284) | 973 (89 to 10606) | | |
| Serotype 19A, n=8, 7 | 652 (131 to 3234) | 435 (14 to 13833) | | |
| Serotype 19F, n=7, 9 | 1570 (239 to 10337) | 701 (124 to 3958) | | |
| Serotype 23F, n=8, 8 | 152 (24 to 966) | 410 (22 to 7594) | | |
| Serotype 8, n=4, 6 | 368 (11 to 12078) | 149 (9 to 2337) | | |
| Serotype 10A, n=4, 6 | 2851 (1309 to 6210) | 117 (15 to 916) | | |
| Serotype 11A, n=4, 4 | 7137 (1036 to 49164) | 1789 (36 to 89068) | | |
| Serotype 12F, n=4, 7 | 757 (15 to 37522) | 241 (16 to 3734) | | |
| Serotype 15B, n=5, 7 | 822 (42 to 16070) | 147 (10 to 2214) | | |
| Serotype 22F, n=4, 7 | 1983 (390 to 10085) | 1635 (165 to 16157) | | |
| Serotype 33F, n=3, 7 | 5903 (53 to 657862) | 3619 (948 to 13817) | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Local reactions & Systemic events [systematic assessment (SA)]: Within 7 days after Dose 1,2, or 3;
SAEs(non-SA): From Dose 1 up to 1 month after Dose 3 & other AEs (non-SAE): From Dose 1 up to 1 month after Dose 2 & from Dose 3 up to 1 month after Dose 3

Adverse event reporting additional description:

Same event may appear as both SAE & non-SAE. However, what is presented are distinct events. Event may be classified as serious in 1 subject & non-serious in another, or 1 subject may have experienced both during study. Safety analysis set evaluated. MedDRA 25.0 was used for primary cohorts and 26.0 was used for Russian cohort.

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

Dictionary used

| | |
|--------------------|--------|
| Dictionary name | MedDRA |
| Dictionary version | 25.0 |

Reporting groups

| | |
|-----------------------|----------------------------------|
| Reporting group title | 20vPnC: Primary Study Population |
|-----------------------|----------------------------------|

Reporting group description:

Infants 42 to 112 days of age were enrolled to receive 3 doses of 0.5 mL 20vPnC intramuscularly. Dose 1 was given at enrollment and Dose 2 was given 42 to 63 days later. Dose 3 was administered at 11 to 12 months of age.

| | |
|-----------------------|------------------------|
| Reporting group title | 13vPnC: Russian Cohort |
|-----------------------|------------------------|

Reporting group description:

Infants 42 to 70 days of age were enrolled to receive 3 doses of 0.5 mL 13vPnC intramuscularly. Dose 1 was given at enrollment and Dose 2 was given 60 to 90 days later. Dose 3 was administered at 28 to 42 days after Dose 2.

| | |
|-----------------------|------------------------|
| Reporting group title | 20vPnC: Russian Cohort |
|-----------------------|------------------------|

Reporting group description:

Infants 42 to 70 days of age were enrolled to receive 3 doses of 0.5 mL 20vPnC intramuscularly. Dose 1 was given at enrollment and Dose 2 was given 60 to 90 days later. Dose 3 was administered at 28 to 42 days after Dose 2

| | |
|-----------------------|----------------------------------|
| Reporting group title | 13vPnC: Primary Study Population |
|-----------------------|----------------------------------|

Reporting group description:

Infants 42 to 112 days of age were enrolled to receive 3 doses of 0.5 mL 13vPnC intramuscularly. Dose 1 was given at enrollment and Dose 2 was given 42 to 63 days later. Dose 3 was administered at 11 to 12 months of age.

| Serious adverse events | 20vPnC: Primary Study Population | 13vPnC: Russian Cohort | 20vPnC: Russian Cohort |
|---|---|------------------------|------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 34 / 601 (5.66%) | 0 / 27 (0.00%) | 0 / 24 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Benign salivary gland neoplasm | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |

| | | | |
|--|---|----------------|----------------|
| subjects affected / exposed | 1 / 601 (0.17%) | 0 / 27 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Inflammation | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 1 / 601 (0.17%) | 0 / 27 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune system disorders | | | |
| Anaphylactic reaction | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 0 / 601 (0.00%) | 0 / 27 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Bronchial hyperreactivity | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 1 / 601 (0.17%) | 0 / 27 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Foreign body aspiration | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 0 / 601 (0.00%) | 0 / 27 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thermal burn | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 1 / 601 (0.17%) | 0 / 27 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skull fracture | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 1 / 601 (0.17%) | 0 / 27 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Congenital, familial and genetic disorders | | | |
| Aorticopulmonary septal defect | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |

| | | | |
|---|---|----------------|----------------|
| subjects affected / exposed | 1 / 601 (0.17%) | 0 / 27 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchogenic cyst | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 1 / 601 (0.17%) | 0 / 27 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Febrile convulsion | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 1 / 601 (0.17%) | 0 / 27 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebral haemorrhage | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 1 / 601 (0.17%) | 0 / 27 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intracranial pressure increased | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 1 / 601 (0.17%) | 0 / 27 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypotonia | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 0 / 601 (0.00%) | 0 / 27 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Seizure | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 0 / 601 (0.00%) | 0 / 27 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Thymus enlargement | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 0 / 601 (0.00%) | 0 / 27 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lymphadenitis | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |

| | | | |
|---|---|----------------|----------------|
| subjects affected / exposed | 1 / 601 (0.17%) | 0 / 27 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neutropenia | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 0 / 601 (0.00%) | 0 / 27 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Colitis | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 0 / 601 (0.00%) | 0 / 27 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| Urticaria | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 0 / 601 (0.00%) | 0 / 27 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dermatitis atopic | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 0 / 601 (0.00%) | 0 / 27 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Nephritis | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 0 / 601 (0.00%) | 0 / 27 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tubulointerstitial nephritis | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 1 / 601 (0.17%) | 0 / 27 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vesicoureteric reflux | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 1 / 601 (0.17%) | 0 / 27 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|---|----------------|----------------|
| Infections and infestations | | | |
| Bacterial infection | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 1 / 601 (0.17%) | 0 / 27 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchiolitis | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 2 / 601 (0.33%) | 0 / 27 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchitis | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 1 / 601 (0.17%) | 0 / 27 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| COVID-19 | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 0 / 601 (0.00%) | 0 / 27 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Erythema infectiosum | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 0 / 601 (0.00%) | 0 / 27 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Escherichia urinary tract infection | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 0 / 601 (0.00%) | 0 / 27 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 4 / 601 (0.67%) | 0 / 27 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis rotavirus | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 0 / 601 (0.00%) | 0 / 27 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lower respiratory tract infection viral | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |

| | | | |
|---|---|----------------|----------------|
| subjects affected / exposed | 0 / 601 (0.00%) | 0 / 27 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal infection | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 2 / 601 (0.33%) | 0 / 27 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal viral infection | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 0 / 601 (0.00%) | 0 / 27 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Herpangina | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 1 / 601 (0.17%) | 0 / 27 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Laryngitis | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 1 / 601 (0.17%) | 0 / 27 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis viral | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 0 / 601 (0.00%) | 0 / 27 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Otitis media | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 0 / 601 (0.00%) | 0 / 27 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oral candidiasis | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 0 / 601 (0.00%) | 0 / 27 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Meningitis enteroviral | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |

| | | | |
|---|---|----------------|----------------|
| subjects affected / exposed | 0 / 601 (0.00%) | 0 / 27 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Meningitis | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 1 / 601 (0.17%) | 0 / 27 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 1 / 601 (0.17%) | 0 / 27 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary tract infection | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 4 / 601 (0.67%) | 0 / 27 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin infection | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 1 / 601 (0.17%) | 0 / 27 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory syncytial virus bronchiolitis | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 2 / 601 (0.33%) | 0 / 27 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyelonephritis acute | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 1 / 601 (0.17%) | 0 / 27 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyelonephritis | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 1 / 601 (0.17%) | 0 / 27 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia respiratory syncytial viral | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |

| | | | |
|---|---|----------------|----------------|
| subjects affected / exposed | 1 / 601 (0.17%) | 0 / 27 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Viral infection | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 3 / 601 (0.50%) | 0 / 27 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Underweight | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 1 / 601 (0.17%) | 0 / 27 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Type 1 diabetes mellitus | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 1 / 601 (0.17%) | 0 / 27 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Poor feeding infant | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 0 / 601 (0.00%) | 0 / 27 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Feeding disorder | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 0 / 601 (0.00%) | 0 / 27 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|---|--|--|
| Serious adverse events | 13vPnC: Primary Study Population | | |
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 40 / 603 (6.63%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Benign salivary gland neoplasm | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |

| | | | |
|--|---|--|--|
| subjects affected / exposed | 0 / 603 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| Inflammation | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 0 / 603 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Immune system disorders | | | |
| Anaphylactic reaction | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 1 / 603 (0.17%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Bronchial hyperreactivity | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 0 / 603 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Injury, poisoning and procedural complications | | | |
| Foreign body aspiration | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 1 / 603 (0.17%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Thermal burn | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 0 / 603 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Skull fracture | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 0 / 603 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Congenital, familial and genetic disorders | | | |
| Aorticopulmonary septal defect | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |

| | | | |
|---|---|--|--|
| subjects affected / exposed | 0 / 603 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Bronchogenic cyst | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 0 / 603 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Febrile convulsion | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 1 / 603 (0.17%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cerebral haemorrhage | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 0 / 603 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Intracranial pressure increased | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 0 / 603 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypotonia | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 1 / 603 (0.17%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Seizure | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 1 / 603 (0.17%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |
| Thymus enlargement | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 1 / 603 (0.17%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Lymphadenitis | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |

| | | | |
|---|---|--|--|
| subjects affected / exposed | 1 / 603 (0.17%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Neutropenia | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 1 / 603 (0.17%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Colitis | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 1 / 603 (0.17%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Skin and subcutaneous tissue disorders | | | |
| Urticaria | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 1 / 603 (0.17%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Dermatitis atopic | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 1 / 603 (0.17%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal and urinary disorders | | | |
| Nephritis | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 1 / 603 (0.17%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Tubulointerstitial nephritis | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 0 / 603 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vesicoureteric reflux | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 0 / 603 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|-----------------------------|---|---|--|
| Infections and infestations | | | |
| | Bacterial infection | Additional description: MedDRA 26.0 was used for Russian Cohorts. | |
| | subjects affected / exposed | 0 / 603 (0.00%) | |
| | occurrences causally related to treatment / all | 0 / 0 | |
| | deaths causally related to treatment / all | 0 / 0 | |
| | Bronchiolitis | Additional description: MedDRA 26.0 was used for Russian Cohorts. | |
| | subjects affected / exposed | 2 / 603 (0.33%) | |
| | occurrences causally related to treatment / all | 0 / 2 | |
| | deaths causally related to treatment / all | 0 / 0 | |
| | Bronchitis | Additional description: MedDRA 26.0 was used for Russian Cohorts. | |
| | subjects affected / exposed | 0 / 603 (0.00%) | |
| | occurrences causally related to treatment / all | 0 / 0 | |
| | deaths causally related to treatment / all | 0 / 0 | |
| | COVID-19 | Additional description: MedDRA 26.0 was used for Russian Cohorts. | |
| | subjects affected / exposed | 1 / 603 (0.17%) | |
| | occurrences causally related to treatment / all | 0 / 1 | |
| | deaths causally related to treatment / all | 0 / 0 | |
| | Erythema infectiosum | Additional description: MedDRA 26.0 was used for Russian Cohorts. | |
| | subjects affected / exposed | 1 / 603 (0.17%) | |
| | occurrences causally related to treatment / all | 0 / 1 | |
| | deaths causally related to treatment / all | 0 / 0 | |
| | Escherichia urinary tract infection | Additional description: MedDRA 26.0 was used for Russian Cohorts. | |
| | subjects affected / exposed | 2 / 603 (0.33%) | |
| | occurrences causally related to treatment / all | 0 / 2 | |
| | deaths causally related to treatment / all | 0 / 0 | |
| | Gastroenteritis | Additional description: MedDRA 26.0 was used for Russian Cohorts. | |
| | subjects affected / exposed | 5 / 603 (0.83%) | |
| | occurrences causally related to treatment / all | 0 / 5 | |
| | deaths causally related to treatment / all | 0 / 0 | |
| | Gastroenteritis rotavirus | Additional description: MedDRA 26.0 was used for Russian Cohorts. | |
| | subjects affected / exposed | 1 / 603 (0.17%) | |
| | occurrences causally related to treatment / all | 0 / 1 | |
| | deaths causally related to treatment / all | 0 / 0 | |
| | Lower respiratory tract infection viral | Additional description: MedDRA 26.0 was used for Russian Cohorts. | |

| | | | |
|---|---|--|--|
| subjects affected / exposed | 1 / 603 (0.17%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal infection | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 2 / 603 (0.33%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal viral infection | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 1 / 603 (0.17%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Herpangina | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 0 / 603 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Laryngitis | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 2 / 603 (0.33%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastroenteritis viral | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 1 / 603 (0.17%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Otitis media | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 1 / 603 (0.17%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Oral candidiasis | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 1 / 603 (0.17%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Meningitis enteroviral | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |

| | | | |
|---|---|--|--|
| subjects affected / exposed | 1 / 603 (0.17%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Meningitis | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 0 / 603 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumonia | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 3 / 603 (0.50%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Urinary tract infection | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 4 / 603 (0.66%) | | |
| occurrences causally related to treatment / all | 0 / 5 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Skin infection | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 0 / 603 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory syncytial virus bronchiolitis | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 1 / 603 (0.17%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pyelonephritis acute | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 1 / 603 (0.17%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pyelonephritis | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 0 / 603 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumonia respiratory syncytial viral | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |

| | | | |
|---|---|--|--|
| subjects affected / exposed | 0 / 603 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Viral infection | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 1 / 603 (0.17%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolism and nutrition disorders | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| Underweight | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 0 / 603 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Type 1 diabetes mellitus | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 0 / 603 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Poor feeding infant | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 1 / 603 (0.17%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Feeding disorder | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 3 / 603 (0.50%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | 20vPnC: Primary Study Population | 13vPnC: Russian Cohort | 20vPnC: Russian Cohort |
|---|---|------------------------|------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 589 / 601 (98.00%) | 20 / 27 (74.07%) | 17 / 24 (70.83%) |
| Nervous system disorders | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| Hypersomnia (INCREASED SLEEP) | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| alternative assessment type: Systematic | | | |

| | | | |
|--|---|------------------------|------------------------|
| subjects affected / exposed occurrences (all) | 495 / 601 (82.36%) 965 | 11 / 27 (40.74%) 16 | 8 / 24 (33.33%) 11 |
| General disorders and administration site conditions | | | |
| Injection site erythema (REDNESS) alternative assessment type: Systematic | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed occurrences (all) | 331 / 601 (55.07%) 534 | 4 / 27 (14.81%) 6 | 3 / 24 (12.50%) 4 |
| Injection site pain (PAIN) alternative assessment type: Systematic | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed occurrences (all) | 343 / 601 (57.07%) 555 | 6 / 27 (22.22%) 7 | 7 / 24 (29.17%) 8 |
| Injection site swelling (SWELLING) alternative assessment type: Systematic | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed occurrences (all) | 260 / 601 (43.26%) 431 | 3 / 27 (11.11%) 3 | 4 / 24 (16.67%) 5 |
| Pyrexia (FEVER) alternative assessment type: Systematic | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed occurrences (all) | 212 / 601 (35.27%) 282 | 4 / 27 (14.81%) 4 | 2 / 24 (8.33%) 3 |
| Psychiatric disorders | | | |
| Irritability (IRRITABILITY) alternative assessment type: Systematic | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed occurrences (all) | 553 / 601 (92.01%) 1266 | 15 / 27 (55.56%) 24 | 13 / 24 (54.17%) 18 |
| Infections and infestations | | | |
| Upper respiratory tract infection | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed occurrences (all) | 21 / 601 (3.49%) 21 | 0 / 27 (0.00%) 0 | 1 / 24 (4.17%) 1 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite (DECREASED APPETITE) alternative assessment type: Systematic | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed occurrences (all) | 345 / 601 (57.40%) 522 | 8 / 27 (29.63%) 10 | 9 / 24 (37.50%) 10 |

| | | | |
|-----------------------------------|-------------------------------------|--|--|
| Non-serious adverse events | 13vPnC: Primary Study Population | | |
|-----------------------------------|-------------------------------------|--|--|

| | | | |
|---|---|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 593 / 603 (98.34%) | | |
| Nervous system disorders | | | |
| Hypersomnia (INCREASED SLEEP) | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 512 / 603 (84.91%) | | |
| occurrences (all) | 970 | | |
| General disorders and administration site conditions | | | |
| Injection site erythema (REDNESS) | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 333 / 603 (55.22%) | | |
| occurrences (all) | 531 | | |
| Injection site pain (PAIN) | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 347 / 603 (57.55%) | | |
| occurrences (all) | 557 | | |
| Injection site swelling (SWELLING) | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 251 / 603 (41.63%) | | |
| occurrences (all) | 388 | | |
| Pyrexia (FEVER) | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 214 / 603 (35.49%) | | |
| occurrences (all) | 273 | | |
| Psychiatric disorders | | | |
| Irritability (IRRITABILITY) | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 556 / 603 (92.21%) | | |
| occurrences (all) | 1258 | | |
| Infections and infestations | | | |
| Upper respiratory tract infection | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| subjects affected / exposed | 35 / 603 (5.80%) | | |
| occurrences (all) | 40 | | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite (DECREASED APPETITE) | Additional description: MedDRA 26.0 was used for Russian Cohorts. | | |
| alternative assessment type: Systematic | | | |

| | | | |
|-----------------------------|--------------------|--|--|
| subjects affected / exposed | 323 / 603 (53.57%) | | |
| occurrences (all) | 465 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|--------------|--|
| 18 June 2021 | amendment 2:Added noninferiority of IgG GMCs and the percentage of participants with predefined thresholds after 2 infant doses as primary immunogenicity objectives and moved objective for IgG percentage of participants with predefined thresholds after toddler dose to secondary objective, based on Scientific Advice from CHMP. The statistical sections for these objectives were updated accordingly. Added country-specific appendix for Russian cohort to add approximately 60 participants and address comments from a national agency on schedule, concomitant vaccines and other study aspects, including management of Russian cohort data. Made updates throughout the protocol on managing the Russian cohort. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported