



Clinical trial results:

A Phase 3, Multicenter, Randomized, Double-blind, Active-comparator-controlled Study to Evaluate the Safety, Tolerability, and Immunogenicity of a 3-dose Regimen of V114 in Healthy Infants (PNEU-PED-EU-2)

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2018-003788-70 |
| Trial protocol | FI NO DK SE IT |
| Global end of trial date | 02 November 2021 |

Results information

| | |
|--------------------------------|-------------|
| Result version number | v1 |
| This version publication date | 13 May 2022 |
| First version publication date | 13 May 2022 |

Trial information

Trial identification

| | |
|-----------------------|----------|
| Sponsor protocol code | V114-026 |
|-----------------------|----------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT04016714 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Merck Sharp & Dohme Corp. |
| Sponsor organisation address | 2000 Galloping Hill Road, Kenilworth, NJ, United States, 07033 |
| Public contact | Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com |
| Scientific contact | Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com |

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

| | |
|--|------------------|
| Analysis stage | Final |
| Date of interim/final analysis | 29 October 2021 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 29 October 2021 |
| Global end of trial reached? | Yes |
| Global end of trial date | 02 November 2021 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study was to evaluate the safety, tolerability, and immunogenicity of a 3-dose schedule (2-dose primary series followed by a toddler dose) of pneumococcal conjugate vaccine (PCV) as one of the currently recommended by the World Health Organization (WHO) Strategic Advisory Group of Experts (SAGE) on Immunizations and practiced in many countries. The primary hypotheses were: V114 is non-inferior to Prevenar 13™ for the 13 shared serotypes based on response rates and on anti-pneumococcal polysaccharide (PnPs) serotype-specific Immunoglobulin G (IgG) geometric mean concentrations (GMCs) 30 days after Dose 3; V114 is superior to Prevenar 13™ for the 2 serotypes unique to V114 based on the response rates and on anti-PnPs serotype-specific IgG GMCs 30 days after Dose 3; and Vaxelis™ administered concomitantly with V114 is non-inferior to Vaxelis™ administered concomitantly with Prevenar 13™ 30 days after Dose 3 for each antigen included in Vaxelis™.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

| | |
|---|----------------|
| Actual start date of recruitment | 28 August 2019 |
| 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 | Denmark: 379 |
| Country: Number of subjects enrolled | Finland: 612 |
| Country: Number of subjects enrolled | Italy: 105 |
| Country: Number of subjects enrolled | Norway: 95 |
| Worldwide total number of subjects | 1191 |
| EEA total number of subjects | 1191 |

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) | 1191 |
| 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:

This study enrolled healthy infants. Other inclusion criteria applied.

Period 1

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

Arms

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

Arm description:

Participants received a single 0.5 mL intramuscular (IM) injection of V114 at Visit 1, 2, and 4 (approximately 3, 5, and 12 months of age). As part of the study design, participants also received other pediatric vaccines, including Vaxelis™ (0.5 mL single dose at Visits 1, 2, and 4); M-M-R™II (0.5 mL single dose at Visit 4); and VARIVAX™ (0.5 mL single dose at Visit 4, except participants in Norway and Denmark, who received a second dose of VARIVAX™ at Visit 5, according to local vaccination requirements).

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

Dosage and administration details:

15-valent pneumococcal conjugate vaccine with serotypes 1, 3, 4, 5, 6A, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F, 33F, serotype 6B and aluminum phosphate adjuvant in each 0.5 mL dose.

| | |
|--|--------------------------|
| Investigational medicinal product name | Varivax™ |
| Investigational medicinal product code | |
| Other name | Varicella Vaccine Live |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

0.5 mL single dose

| | |
|--|--|
| Investigational medicinal product name | M-M-R™II |
| Investigational medicinal product code | |
| Other name | Measles, Mumps, and Rubella Virus Vaccine Live |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

0.5 mL single dose

| | |
|--|--------------------------|
| Investigational medicinal product name | Vaxelis™ |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

0.5 mL single dose

| | |
|------------------|--------------|
| Arm title | Prevenar 13™ |
|------------------|--------------|

Arm description:

Participants received a single 0.5 mL IM injection of Prevenar 13™ at Visit 1, 2, and 4 (approximately 3, 5, and 12 months of age). As part of the study design, participants also received other pediatric vaccines, including Vaxelis™ (0.5 mL single dose at Visits 1, 2, and 4); M-M-R™II (0.5 mL single dose at Visit 4); and VARIVAX™ (0.5 mL single dose at Visit 4, except participants in Norway and Denmark, who received a second dose of VARIVAX™ at Visit 5, according to local vaccination requirements).

| | |
|--|--|
| Arm type | Active comparator |
| Investigational medicinal product name | Prevenar 13™ |
| Investigational medicinal product code | |
| Other name | Pneumococcal 13-valent Conjugate Vaccine |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

13-valent pneumococcal capsular polysaccharide with serotypes 1, 3, 4, 5, 6A, 7F, 9V, 14, 18C, 19A, 19F, 23F (2.2 mcg) and 6B (4.4 mcg) in each 0.5 ml dose

| | |
|--|--------------------------|
| Investigational medicinal product name | Varivax™ |
| Investigational medicinal product code | |
| Other name | Varicella Vaccine Live |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

0.5 mL single dose

| | |
|--|--|
| Investigational medicinal product name | M-M-R™II |
| Investigational medicinal product code | |
| Other name | Measles, Mumps, and Rubella Virus Vaccine Live |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

0.5 mL single dose

| | |
|--|--------------------------|
| Investigational medicinal product name | Vaxelis™ |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

0.5 mL single dose

| Number of subjects in period 1 | V114 | Prevenar 13™ |
|---------------------------------------|------|--------------|
| Started | 595 | 596 |
| Vaccination 1 (V114 or Prevenar 13™) | 595 | 596 |
| Vaccination 2 (V114 or Prevenar 13™) | 585 | 588 |
| Vaccination 3 (V114 or Prevenar 13™) | 573 | 581 |

| | | |
|-------------------------------|-----|-----|
| Completed | 572 | 580 |
| Not completed | 23 | 16 |
| Physician decision | 3 | 3 |
| Death | 1 | - |
| Withdrawal by Parent/Guardian | 16 | 12 |
| Lost to follow-up | 3 | 1 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|------|
| Reporting group title | V114 |
|-----------------------|------|

Reporting group description:

Participants received a single 0.5 mL intramuscular (IM) injection of V114 at Visit 1, 2, and 4 (approximately 3, 5, and 12 months of age). As part of the study design, participants also received other pediatric vaccines, including Vaxelis™ (0.5 mL single dose at Visits 1, 2, and 4); M-M-R™II (0.5 mL single dose at Visit 4); and VARIVAX™ (0.5 mL single dose at Visit 4, except participants in Norway and Denmark, who received a second dose of VARIVAX™ at Visit 5, according to local vaccination requirements).

| | |
|-----------------------|--------------|
| Reporting group title | Prevenar 13™ |
|-----------------------|--------------|

Reporting group description:

Participants received a single 0.5 mL IM injection of Prevenar 13™ at Visit 1, 2, and 4 (approximately 3, 5, and 12 months of age). As part of the study design, participants also received other pediatric vaccines, including Vaxelis™ (0.5 mL single dose at Visits 1, 2, and 4); M-M-R™II (0.5 mL single dose at Visit 4); and VARIVAX™ (0.5 mL single dose at Visit 4, except participants in Norway and Denmark, who received a second dose of VARIVAX™ at Visit 5, according to local vaccination requirements).

| Reporting group values | V114 | Prevenar 13™ | Total |
|---|-------|--------------|-------|
| Number of subjects | 595 | 596 | 1191 |
| Age Categorical Units: Participants | | | |
| 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) | 595 | 596 | 1191 |
| 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: weeks | | | |
| arithmetic mean | 12.4 | 12.5 | |
| standard deviation | ± 1.4 | ± 1.4 | - |
| Gender Categorical Units: Participants | | | |
| Female | 272 | 289 | 561 |
| Male | 323 | 307 | 630 |
| Race Units: Subjects | | | |
| American Indian or Alaska Native | 1 | 1 | 2 |
| Asian | 2 | 4 | 6 |
| Multiple | 13 | 12 | 25 |
| White | 579 | 579 | 1158 |
| Ethnicity Units: Subjects | | | |
| Hispanic or Latino | 26 | 22 | 48 |
| Not Hispanic or Latino | 564 | 570 | 1134 |

| | | | |
|--------------|---|---|---|
| Not Reported | 3 | 3 | 6 |
| Unknown | 2 | 1 | 3 |

End points

End points reporting groups

| | |
|---|--------------|
| Reporting group title | V114 |
| Reporting group description: | |
| Participants received a single 0.5 mL intramuscular (IM) injection of V114 at Visit 1, 2, and 4 (approximately 3, 5, and 12 months of age). As part of the study design, participants also received other pediatric vaccines, including Vaxelis™ (0.5 mL single dose at Visits 1, 2, and 4); M-M-R™II (0.5 mL single dose at Visit 4); and VARIVAX™ (0.5 mL single dose at Visit 4, except participants in Norway and Denmark, who received a second dose of VARIVAX™ at Visit 5, according to local vaccination requirements). | |
| Reporting group title | Prevenar 13™ |
| Reporting group description: | |
| Participants received a single 0.5 mL IM injection of Prevenar 13™ at Visit 1, 2, and 4 (approximately 3, 5, and 12 months of age). As part of the study design, participants also received other pediatric vaccines, including Vaxelis™ (0.5 mL single dose at Visits 1, 2, and 4); M-M-R™II (0.5 mL single dose at Visit 4); and VARIVAX™ (0.5 mL single dose at Visit 4, except participants in Norway and Denmark, who received a second dose of VARIVAX™ at Visit 5, according to local vaccination requirements). | |

Primary: Percentage of Participants with a Solicited Injection-site Adverse Event

| | |
|---|--|
| End point title | Percentage of Participants with a Solicited Injection-site Adverse Event |
| End point description: | |
| An adverse event (AE) is any untoward medical occurrence in a clinical study participant, temporally associated with the use of study treatment, whether or not considered related to the study treatment. Solicited injection-site AEs included injection-site erythema (redness), injection-site induration (hard lump), injection-site pain (tenderness), and injection-site swelling. The analysis population for this endpoint included all randomized participants who received at least 1 dose of study vaccination. | |
| End point type | Primary |
| End point timeframe: | |
| Day 1 to Day 14 after each vaccination | |

| End point values | V114 | Prevenar 13™ | | |
|-----------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 595 | 594 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| Injection-site erythema | 60.0 | 65.5 | | |
| Injection-site induration | 57.0 | 59.1 | | |
| Injection-site pain | 63.0 | 59.6 | | |
| Injection-site swelling | 46.4 | 44.1 | | |

Statistical analyses

| | |
|----------------------------|-------------------------|
| Statistical analysis title | Injection-site erythema |
| Comparison groups | V114 v Prevenar 13™ |

| | |
|---|--|
| Number of subjects included in analysis | 1189 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.05 |
| Method | Miettinen & Nurminen method |
| Parameter estimate | Difference in percentage vs Prevenar 13™ |
| Point estimate | -5.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -11 |
| upper limit | 0 |

| | |
|---|--|
| Statistical analysis title | Injection-site induration |
| Comparison groups | V114 v Prevenar 13™ |
| Number of subjects included in analysis | 1189 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.46 |
| Method | Miettinen & Nurminen method |
| Parameter estimate | Difference in percentage vs Prevenar 13™ |
| Point estimate | -2.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -7.7 |
| upper limit | 3.5 |

| | |
|---|--|
| Statistical analysis title | Injection-site pain |
| Comparison groups | V114 v Prevenar 13™ |
| Number of subjects included in analysis | 1189 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.225 |
| Method | Miettinen & Nurminen method |
| Parameter estimate | Difference in percentage vs Prevenar 13™ |
| Point estimate | 3.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.1 |
| upper limit | 8.9 |

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

| | |
|---|--|
| Comparison groups | V114 v Prevenar 13™ |
| Number of subjects included in analysis | 1189 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.43 |
| Method | Miettinen & Nurminen method |
| Parameter estimate | Difference in percentage vs Prevenar 13™ |
| Point estimate | 2.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.4 |
| upper limit | 7.9 |

Primary: Percentage of Participants with a Solicited Systemic Adverse Event

| | |
|---|--|
| End point title | Percentage of Participants with a Solicited Systemic Adverse Event |
| End point description: | |
| An AE is any untoward medical occurrence in a clinical study participant, temporally associated with the use of study treatment, whether or not considered related to the study treatment. Solicited systemic AEs included decreased appetite, irritability, somnolence (drowsiness), and urticaria (hives or welts). The analysis population for this endpoint included all randomized participants who received at least 1 dose of study vaccination. | |
| End point type | Primary |
| End point timeframe: | |
| Day 1 to Day 14 after each vaccination | |

| End point values | V114 | Prevenar 13™ | | |
|-----------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 595 | 594 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| Decreased appetite | 54.8 | 58.2 | | |
| Irritability | 96.3 | 94.1 | | |
| Somnolence | 77.3 | 77.9 | | |
| Urticaria | 16.8 | 21.4 | | |

Statistical analyses

| | |
|----------------------------|---------------------|
| Statistical analysis title | Decreased appetite |
| Comparison groups | V114 v Prevenar 13™ |

| | |
|---|--|
| Number of subjects included in analysis | 1189 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.229 |
| Method | Miettinen & Nurminen method |
| Parameter estimate | Difference in percentage vs Prevenar 13™ |
| Point estimate | -3.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -9.1 |
| upper limit | 2.2 |

| | |
|---|--|
| Statistical analysis title | Irritability |
| Comparison groups | V114 v Prevenar 13™ |
| Number of subjects included in analysis | 1189 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.077 |
| Method | Miettinen & Nurminen method |
| Parameter estimate | Difference in percentage vs Prevenar 13™ |
| Point estimate | 2.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.2 |
| upper limit | 4.7 |

| | |
|---|--|
| Statistical analysis title | Somnolence |
| Comparison groups | V114 v Prevenar 13™ |
| Number of subjects included in analysis | 1189 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.793 |
| Method | Miettinen & Nurminen method |
| Parameter estimate | Difference in percentage vs Prevenar 13™ |
| Point estimate | -0.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -5.4 |
| upper limit | 4.1 |

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

| | |
|---|--|
| Comparison groups | V114 v Prevenar 13™ |
| Number of subjects included in analysis | 1189 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.045 |
| Method | Miettinen & Nurminen method |
| Parameter estimate | Difference in percentage vs Prevenar 13™ |
| Point estimate | -4.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -9.1 |
| upper limit | -0.1 |

Primary: Percentage of Participants with a Vaccine-related Serious Adverse Event

| | |
|-----------------|---|
| End point title | Percentage of Participants with a Vaccine-related Serious Adverse Event |
|-----------------|---|

End point description:

A serious adverse event (SAE) is an AE that results in death, is life-threatening, requires or prolongs an existing hospitalization, results in persistent or significant disability or incapacity, is a congenital anomaly or birth defect, or is another important medical event deemed such by medical or scientific judgment. SAEs that were reported by the investigator to be at least possibly related to the study vaccination were summarized. The analysis population for this endpoint included all randomized participants who received at least 1 dose of study vaccination.

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

End point timeframe:

Up to approximately 6 months after Dose 3 (up to approximately 16 months)

| End point values | V114 | Prevenar 13™ | | |
|-----------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 595 | 594 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 0.3 | 0.3 | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Vaccine-related SAEs |
| Comparison groups | V114 v Prevenar 13™ |
| Number of subjects included in analysis | 1189 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Method | Miettinen & Nurminen method |
| Parameter estimate | Difference in percentage vs Prevenar 13™ |
| Point estimate | 0 |

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

Primary: Percentage of Participants Meeting Serotype-specific Immunoglobulin G (IgG) Threshold Value of ≥ 0.35 $\mu\text{g/mL}$ 30 Days after Dose 3

| | |
|-----------------|--|
| End point title | Percentage of Participants Meeting Serotype-specific Immunoglobulin G (IgG) Threshold Value of ≥ 0.35 $\mu\text{g/mL}$ 30 Days after Dose 3 |
|-----------------|--|

End point description:

The GMC of IgG serotype-specific antibodies to the 13 serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F) included in V114 and Prevenar 13™ and 2 serotypes (22F and 33F) unique to V114 were quantitated from participants' sera by a multiplex electrochemiluminescence (ECL) assay. Immunoglobulin G for the 15 serotypes contained in V114 vaccine was determined using a pneumococcal electrochemiluminescence (PnECL) assay. The analysis population for this endpoint included all randomized participants without protocol deviations that could have substantially impacted the results of the immunogenicity analyses and who had sufficient data to perform the analysis for each serotype.

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

End point timeframe:

30 days after Dose 3

| End point values | V114 | Prevenar 13™ | | |
|-----------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 500 | 525 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| Serotype 1 (n=500, 525) | 96.8 | 99.0 | | |
| Serotype 3 (n=500, 525) | 92.8 | 82.3 | | |
| Serotype 4 (n=500, 523) | 96.6 | 98.5 | | |
| Serotype 5 (n=500, 524) | 99.4 | 99.6 | | |
| Serotype 6A (n=500, 523) | 99.2 | 99.4 | | |
| Serotype 6B (n=500, 523) | 99.2 | 99.0 | | |
| Serotype 7F (n=500, 525) | 100.0 | 99.6 | | |
| Serotype 9V (n=499, 525) | 99.8 | 99.6 | | |
| Serotype 14 (n=500, 523) | 99.2 | 99.6 | | |
| Serotype 18C (n=500, 525) | 99.8 | 99.4 | | |
| Serotype 19A (n=500, 523) | 99.6 | 99.8 | | |
| Serotype 19F (n=500, 524) | 99.8 | 99.6 | | |
| Serotype 23F (n=497, 521) | 97.8 | 96.9 | | |
| Serotype 22F (n=500, 520) | 99.4 | 5.4 | | |
| Serotype 33F (n=500, 510) | 99.2 | 2.0 | | |

Statistical analyses

| | |
|---|-----------------------------|
| Statistical analysis title | Serotype 1 |
| Comparison groups | V114 v Prevenar 13™ |
| Number of subjects included in analysis | 1025 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | < 0.001 |
| Method | Miettinen & Nurminen method |
| Parameter estimate | Percentage point difference |
| Point estimate | -2.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -4.3 |
| upper limit | -0.6 |

| | |
|---|-----------------------------|
| Statistical analysis title | Serotype 3 |
| Comparison groups | V114 v Prevenar 13™ |
| Number of subjects included in analysis | 1025 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | < 0.001 |
| Method | Miettinen & Nurminen method |
| Parameter estimate | Percentage point difference |
| Point estimate | 10.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 6.6 |
| upper limit | 14.6 |

| | |
|---|-----------------------------|
| Statistical analysis title | Serotype 4 |
| Comparison groups | V114 v Prevenar 13™ |
| Number of subjects included in analysis | 1025 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | < 0.001 |
| Method | Miettinen & Nurminen method |
| Parameter estimate | Percentage point difference |
| Point estimate | -1.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -4 |
| upper limit | 0 |

| | |
|---|-----------------------------|
| Statistical analysis title | Serotype 5 |
| Comparison groups | V114 v Prevenar 13™ |
| Number of subjects included in analysis | 1025 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | < 0.001 |
| Method | Miettinen & Nurminen method |
| Parameter estimate | Percentage point difference |
| Point estimate | -0.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.4 |
| upper limit | 0.8 |

| | |
|---|-----------------------------|
| Statistical analysis title | Serotype 6A |
| Comparison groups | V114 v Prevenar 13™ |
| Number of subjects included in analysis | 1025 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | < 0.001 |
| Method | Miettinen & Nurminen method |
| Parameter estimate | Percentage point difference |
| Point estimate | -0.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.5 |
| upper limit | 1 |

| | |
|---|-----------------------------|
| Statistical analysis title | Serotype 6B |
| Comparison groups | V114 v Prevenar 13™ |
| Number of subjects included in analysis | 1025 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | < 0.001 |
| Method | Miettinen & Nurminen method |
| Parameter estimate | Percentage point difference |
| Point estimate | 0.2 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.2 |
| upper limit | 1.5 |

| | |
|---|-----------------------------|
| Statistical analysis title | Serotype 7F |
| Comparison groups | V114 v Prevenar 13™ |
| Number of subjects included in analysis | 1025 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | < 0.001 |
| Method | Miettinen & Nurminen method |
| Parameter estimate | Percentage point difference |
| Point estimate | 0.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.4 |
| upper limit | 1.4 |

| | |
|---|-----------------------------|
| Statistical analysis title | Serotype 9V |
| Comparison groups | V114 v Prevenar 13™ |
| Number of subjects included in analysis | 1025 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | < 0.001 |
| Method | Miettinen & Nurminen method |
| Parameter estimate | Percentage point difference |
| Point estimate | 0.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.8 |
| upper limit | 1.2 |

| | |
|-----------------------------------|---------------------|
| Statistical analysis title | Serotype 14 |
| Comparison groups | V114 v Prevenar 13™ |

| | |
|---|-----------------------------|
| Number of subjects included in analysis | 1025 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | < 0.001 |
| Method | Miettinen & Nurminen method |
| Parameter estimate | Percentage point difference |
| Point estimate | -0.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.7 |
| upper limit | 0.7 |

| | |
|---|-----------------------------|
| Statistical analysis title | Serotype 18C |
| Comparison groups | V114 v Prevenar 13™ |
| Number of subjects included in analysis | 1025 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | < 0.001 |
| Method | Miettinen & Nurminen method |
| Parameter estimate | Percentage point difference |
| Point estimate | 0.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.6 |
| upper limit | 1.5 |

| | |
|---|-----------------------------|
| Statistical analysis title | Serotype 19A |
| Comparison groups | V114 v Prevenar 13™ |
| Number of subjects included in analysis | 1025 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | < 0.001 |
| Method | Miettinen & Nurminen method |
| Parameter estimate | Percentage point difference |
| Point estimate | -0.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.3 |
| upper limit | 0.7 |

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

| | |
|---|-----------------------------|
| Comparison groups | V114 v Prevenar 13™ |
| Number of subjects included in analysis | 1025 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | < 0.001 |
| Method | Miettinen & Nurminen method |
| Parameter estimate | Percentage point difference |
| Point estimate | 0.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.8 |
| upper limit | 1.2 |

| | |
|---|-----------------------------|
| Statistical analysis title | Serotype 23F |
| Comparison groups | V114 v Prevenar 13™ |
| Number of subjects included in analysis | 1025 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | < 0.001 |
| Method | Miettinen & Nurminen method |
| Parameter estimate | Percentage point difference |
| Point estimate | 0.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.2 |
| upper limit | 3 |

| | |
|---|-----------------------------|
| Statistical analysis title | Serotype 22F |
| Comparison groups | V114 v Prevenar 13™ |
| Number of subjects included in analysis | 1025 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Miettinen & Nurminen method |
| Parameter estimate | Percentage point difference |
| Point estimate | 94 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 91.6 |
| upper limit | 95.8 |

| | |
|---|-----------------------------|
| Statistical analysis title | Serotype 33F |
| Comparison groups | V114 v Prevenar 13™ |
| Number of subjects included in analysis | 1025 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | Miettinen & Nurminen method |
| Parameter estimate | Percentage point difference |
| Point estimate | 97.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 95.4 |
| upper limit | 98.4 |

Primary: Geometric Mean Concentration (GMC) of Serotype-specific Immunoglobulin G (IgG) 30 Days after Dose 3

| | |
|---|---|
| End point title | Geometric Mean Concentration (GMC) of Serotype-specific Immunoglobulin G (IgG) 30 Days after Dose 3 |
| End point description: | |
| The GMC of IgG serotype-specific antibodies to the 13 serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F) included in V114 and Prevenar 13™ and 2 serotypes (22F and 33F) unique to V114 were quantitated from participants' sera by a multiplex electrochemiluminescence (ECL) assay. The analysis population for this endpoint included all randomized participants without protocol deviations that could have substantially impacted the results of the immunogenicity analyses and who had sufficient data to perform the analysis for each serotype. | |
| End point type | Primary |
| End point timeframe: | |
| 30 days after Dose 3 | |

| End point values | V114 | Prevenar 13™ | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 500 | 525 | | |
| Units: µg/mL | | | | |
| number (not applicable) | | | | |
| Serotype 1 (n=500, 525) | 1.28 | 2.20 | | |
| Serotype 3 (n=500, 525) | 0.85 | 0.65 | | |
| Serotype 4 (n=500, 523) | 1.41 | 2.00 | | |
| Serotype 5 (n=500, 524) | 2.08 | 3.35 | | |
| Serotype 6A (n=500, 523) | 3.21 | 5.36 | | |
| Serotype 6B (n=500, 523) | 4.56 | 5.12 | | |
| Serotype 7F (n=500, 525) | 2.78 | 3.74 | | |
| Serotype 9V (n=499, 525) | 2.14 | 3.07 | | |
| Serotype 14 (n=500, 523) | 5.35 | 6.83 | | |
| Serotype 18C (n=500, 525) | 2.10 | 2.48 | | |
| Serotype 19A (n=500, 523) | 4.74 | 6.38 | | |
| Serotype 19F (n=500, 524) | 4.08 | 5.18 | | |

| | | | | |
|---------------------------|------|------|--|--|
| Serotype 23F (n=497, 521) | 1.58 | 1.77 | | |
| Serotype 22F (n=500, 520) | 6.06 | 0.09 | | |
| Serotype 33F (n=500, 510) | 3.28 | 0.07 | | |

Statistical analyses

| | |
|---|---------------------|
| Statistical analysis title | Serotype 1 |
| Comparison groups | V114 v Prevenar 13™ |
| Number of subjects included in analysis | 1025 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | < 0.001 |
| Method | t-test, 1-sided |
| Parameter estimate | GMC ratio |
| Point estimate | 0.58 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.54 |
| upper limit | 0.63 |

| | |
|---|---------------------|
| Statistical analysis title | Serotype 3 |
| Comparison groups | V114 v Prevenar 13™ |
| Number of subjects included in analysis | 1025 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | < 0.001 |
| Method | t-test, 1-sided |
| Parameter estimate | GMC ratio |
| Point estimate | 1.31 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.2 |
| upper limit | 1.43 |

| | |
|-----------------------------------|---------------------|
| Statistical analysis title | Serotype 4 |
| Comparison groups | V114 v Prevenar 13™ |

| | |
|---|-----------------|
| Number of subjects included in analysis | 1025 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | < 0.001 |
| Method | t-test, 1-sided |
| Parameter estimate | GMC ratio |
| Point estimate | 0.7 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.63 |
| upper limit | 0.78 |

| | |
|---|---------------------|
| Statistical analysis title | Serotype 5 |
| Comparison groups | V114 v Prevenar 13™ |
| Number of subjects included in analysis | 1025 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | < 0.001 |
| Method | t-test, 1-sided |
| Parameter estimate | GMC ratio |
| Point estimate | 0.62 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.56 |
| upper limit | 0.68 |

| | |
|---|---------------------|
| Statistical analysis title | Serotype 6A |
| Comparison groups | V114 v Prevenar 13™ |
| Number of subjects included in analysis | 1025 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | < 0.001 |
| Method | t-test, 1-sided |
| Parameter estimate | GMC ratio |
| Point estimate | 0.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.54 |
| upper limit | 0.67 |

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

| | |
|---|---------------------|
| Comparison groups | V114 v Prevenar 13™ |
| Number of subjects included in analysis | 1025 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | < 0.001 |
| Method | t-test, 1-sided |
| Parameter estimate | GMC ratio |
| Point estimate | 0.89 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.79 |
| upper limit | 1 |

| | |
|---|---------------------|
| Statistical analysis title | Serotype 7F |
| Comparison groups | V114 v Prevenar 13™ |
| Number of subjects included in analysis | 1025 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | < 0.001 |
| Method | t-test, 1-sided |
| Parameter estimate | GMC ratio |
| Point estimate | 0.74 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.69 |
| upper limit | 0.81 |

| | |
|---|---------------------|
| Statistical analysis title | Serotype 9V |
| Comparison groups | V114 v Prevenar 13™ |
| Number of subjects included in analysis | 1025 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | < 0.001 |
| Method | t-test, 1-sided |
| Parameter estimate | GMC ratio |
| Point estimate | 0.7 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.64 |
| upper limit | 0.76 |

| | |
|---|---------------------|
| Statistical analysis title | Serotype 14 |
| Comparison groups | V114 v Prevenar 13™ |
| Number of subjects included in analysis | 1025 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | < 0.001 |
| Method | t-test, 1-sided |
| Parameter estimate | GMC ratio |
| Point estimate | 0.78 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.7 |
| upper limit | 0.87 |

| | |
|---|---------------------|
| Statistical analysis title | Serotype 18C |
| Comparison groups | V114 v Prevenar 13™ |
| Number of subjects included in analysis | 1025 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | < 0.001 |
| Method | t-test, 1-sided |
| Parameter estimate | GMC ratio |
| Point estimate | 0.85 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.77 |
| upper limit | 0.92 |

| | |
|---|---------------------|
| Statistical analysis title | Serotype 19A |
| Comparison groups | V114 v Prevenar 13™ |
| Number of subjects included in analysis | 1025 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | < 0.001 |
| Method | t-test, 1-sided |
| Parameter estimate | GMC ratio |
| Point estimate | 0.74 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.68 |
| upper limit | 0.82 |

| | |
|---|---------------------|
| Statistical analysis title | Serotype 19F |
| Comparison groups | V114 v Prevenar 13™ |
| Number of subjects included in analysis | 1025 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | < 0.001 |
| Method | t-test, 1-sided |
| Parameter estimate | GMC ratio |
| Point estimate | 0.79 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.72 |
| upper limit | 0.87 |

| | |
|---|---------------------|
| Statistical analysis title | Serotype 23F |
| Comparison groups | V114 v Prevenar 13™ |
| Number of subjects included in analysis | 1025 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | < 0.001 |
| Method | t-test, 1-sided |
| Parameter estimate | GMC ratio |
| Point estimate | 0.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.81 |
| upper limit | 1 |

| | |
|---|---------------------|
| Statistical analysis title | Serotype 22F |
| Comparison groups | V114 v Prevenar 13™ |
| Number of subjects included in analysis | 1025 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | t-test, 1-sided |
| Parameter estimate | GMC ratio |
| Point estimate | 68.34 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 61.73 |
| upper limit | 75.65 |

| | |
|---|---------------------|
| Statistical analysis title | Serotype 33F |
| Comparison groups | V114 v Prevenar 13™ |
| Number of subjects included in analysis | 1025 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.001 |
| Method | t-test, 1-sided |
| Parameter estimate | GMC ratio |
| Point estimate | 48.99 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 44.45 |
| upper limit | 54.01 |

Secondary: Percentage of Participants Meeting Specified Vaxelis™ Antigen Responses 30 Days after Dose 3

| | |
|-----------------|--|
| End point title | Percentage of Participants Meeting Specified Vaxelis™ Antigen Responses 30 Days after Dose 3 |
|-----------------|--|

End point description:

Antigen-specific response rates in participants administered V114 concomitantly with Vaxelis™ were compared with response rates in participants administered Prevenar 13™ concomitantly with Vaxelis™, and the percentages of participants meeting specified Vaxelis™ antigen responses recorded. Antigens in Vaxelis™ include: diphtheria toxoid, tetanus toxoid, pertussis toxin (PT), pertussis filamentous hemagglutinin (FHA), pertussis fimbriae 2/3 (FIM 2/3), pertussis pertactin (PRN), Haemophilus influenzae type b polyribosylribitol phosphate (Hib-PRP), hepatitis B surface antigen (HBsAg), and poliovirus serotypes 1, 2, and 3. The analysis population for this endpoint included all randomized participants without protocol deviations that could have substantially impacted the results of the immunogenicity analyses and who had sufficient data to perform the analysis for each serotype.

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

End point timeframe:

30 days after Dose 3

| | | | | |
|--|-----------------|-----------------|--|--|
| End point values | V114 | Prevenar 13™ | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 500 | 525 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| Diphtheria toxoid: % ≥0.1 IU/mL (n=514, 543) | 100.0 | 99.8 | | |

| | | | | |
|---|-------|-------|--|--|
| Tetanus toxoid: % ≥ 0.1 IU/mL (n=514, 543) | 100.0 | 99.8 | | |
| Pertussis - PT: % ≥ 5 EU/mL (n=514, 543) | 100.0 | 99.8 | | |
| Pertussis - FHA: % ≥ 5 EU/mL (n=514, 543) | 100.0 | 99.8 | | |
| Pertussis - FIM 2/3: % ≥ 20 EU/mL (n=514, 543) | 99.8 | 99.6 | | |
| Pertussis - PRN: % ≥ 5 EU/mL (n=514, 543) | 99.8 | 99.6 | | |
| Hib-PRP: % ≥ 0.15 μ g/mL (n=495, 523) | 96.8 | 97.9 | | |
| HBsAg: % ≥ 10 mIU/mL (n=495, 523) | 99.0 | 99.6 | | |
| Poliovirus 1: % w/ Nab $\geq 1:8$ dilution (n=502, 529) | 99.8 | 99.8 | | |
| Poliovirus 2: % w/ Nab $\geq 1:8$ dilution (n=499, 518) | 100.0 | 99.8 | | |
| Poliovirus 3: % w/ Nab $\geq 1:8$ dilution (n=503, 529) | 100.0 | 100.0 | | |

Statistical analyses

| | |
|---|-----------------------------|
| Statistical analysis title | Diphtheria toxoid |
| Comparison groups | V114 v Prevenar 13™ |
| Number of subjects included in analysis | 1025 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | < 0.001 |
| Method | Miettinen & Nurminen method |
| Parameter estimate | Percentage point difference |
| Point estimate | 0.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.6 |
| upper limit | 1 |

| | |
|---|-----------------------------|
| Statistical analysis title | Tetanus toxoid |
| Comparison groups | V114 v Prevenar 13™ |
| Number of subjects included in analysis | 1025 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | < 0.001 |
| Method | Miettinen & Nurminen method |
| Parameter estimate | Percentage point difference |
| Point estimate | 0.2 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.6 |
| upper limit | 1 |

| | |
|---|-----------------------------|
| Statistical analysis title | Pertussis - PT |
| Comparison groups | V114 v Prevenar 13™ |
| Number of subjects included in analysis | 1025 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | < 0.001 |
| Method | Miettinen & Nurminen method |
| Parameter estimate | Percentage point difference |
| Point estimate | 0.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.6 |
| upper limit | 1 |

| | |
|---|-----------------------------|
| Statistical analysis title | Pertussis - FHA |
| Comparison groups | V114 v Prevenar 13™ |
| Number of subjects included in analysis | 1025 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | < 0.001 |
| Method | Miettinen & Nurminen method |
| Parameter estimate | Percentage point difference |
| Point estimate | 0.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.6 |
| upper limit | 1 |

| | |
|-----------------------------------|---------------------|
| Statistical analysis title | Pertussis - FIM 2/3 |
| Comparison groups | V114 v Prevenar 13™ |

| | |
|---|-----------------------------|
| Number of subjects included in analysis | 1025 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | < 0.001 |
| Method | Miettinen & Nurminen method |
| Parameter estimate | Percentage point difference |
| Point estimate | 0.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.8 |
| upper limit | 1.2 |

| | |
|---|-----------------------------|
| Statistical analysis title | Pertussis - PRN |
| Comparison groups | V114 v Prevenar 13™ |
| Number of subjects included in analysis | 1025 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | < 0.001 |
| Method | Miettinen & Nurminen method |
| Parameter estimate | Percentage point difference |
| Point estimate | 0.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.8 |
| upper limit | 1.2 |

| | |
|---|-----------------------------|
| Statistical analysis title | Hib-PRP |
| Comparison groups | V114 v Prevenar 13™ |
| Number of subjects included in analysis | 1025 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | < 0.001 |
| Method | Miettinen & Nurminen method |
| Parameter estimate | Percentage point difference |
| Point estimate | -1.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.3 |
| upper limit | 0.9 |

| | |
|-----------------------------------|-------|
| Statistical analysis title | HBsAg |
|-----------------------------------|-------|

| | |
|---|-----------------------------|
| Comparison groups | V114 v Prevenar 13™ |
| Number of subjects included in analysis | 1025 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | < 0.001 |
| Method | Miettinen & Nurminen method |
| Parameter estimate | Percentage point difference |
| Point estimate | -0.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2 |
| upper limit | 0.5 |

| | |
|---|-----------------------------|
| Statistical analysis title | Poliovirus 1 |
| Comparison groups | V114 v Prevenar 13™ |
| Number of subjects included in analysis | 1025 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | < 0.001 |
| Method | Miettinen & Nurminen method |
| Parameter estimate | Percentage point difference |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.9 |
| upper limit | 0.9 |

| | |
|---|-----------------------------|
| Statistical analysis title | Poliovirus 2 |
| Comparison groups | V114 v Prevenar 13™ |
| Number of subjects included in analysis | 1025 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | < 0.001 |
| Method | Miettinen & Nurminen method |
| Parameter estimate | Percentage point difference |
| Point estimate | 0.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.6 |
| upper limit | 1.1 |

| | |
|---|-----------------------------|
| Statistical analysis title | Poliovirus 3 |
| Comparison groups | V114 v Prevenar 13™ |
| Number of subjects included in analysis | 1025 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | < 0.001 |
| Method | Miettinen & Nurminen method |
| Parameter estimate | Percentage point difference |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.8 |
| upper limit | 0.7 |

Secondary: Percentage of Participants Meeting Serotype-specific IgG Threshold Value of ≥ 0.35 µg/mL 30 Days after Dose 2

| | |
|--|--|
| End point title | Percentage of Participants Meeting Serotype-specific IgG Threshold Value of ≥ 0.35 µg/mL 30 Days after Dose 2 |
| End point description: The GMC of IgG serotype-specific antibodies to the 13 serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F) included in V114 and Prevenar 13™ and 2 serotypes (22F and 33F) unique to V114 were quantitated from participants' sera by a multiplex ECL assay. Immunoglobulin G for the 15 serotypes contained in V114 vaccine was determined using a PnECL assay. The analysis population for this endpoint included all randomized participants without protocol deviations that could have substantially impacted the results of the immunogenicity analyses and who had sufficient data to perform the analysis for each serotype. | |
| End point type | Secondary |
| End point timeframe: 30 days after Dose 2 | |

| End point values | V114 | Prevenar 13™ | | |
|-----------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 505 | 499 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| Serotype 1 (n=505, 499) | 97.2 | 98.2 | | |
| Serotype 3 (n=505, 499) | 96.8 | 78.0 | | |
| Serotype 4 (n=505, 498) | 97.6 | 98.2 | | |
| Serotype 5 (n=505, 498) | 92.1 | 91.2 | | |
| Serotype 6A (n=505, 498) | 77.2 | 91.4 | | |
| Serotype 6B (n=505, 499) | 59.0 | 40.3 | | |
| Serotype 7F (n=505, 499) | 98.6 | 99.8 | | |
| Serotype 9V (n=504, 498) | 94.0 | 94.8 | | |
| Serotype 14 (n=504, 498) | 96.6 | 96.0 | | |
| Serotype 18C (n=505, 499) | 93.1 | 94.4 | | |
| Serotype 19A (n=505, 499) | 94.1 | 96.6 | | |
| Serotype 19F (n=505, 499) | 98.0 | 99.4 | | |

| | | | | |
|---------------------------|------|------|--|--|
| Serotype 23F (n=505, 498) | 75.4 | 66.7 | | |
| Serotype 22F (n=505, 499) | 97.8 | 2.0 | | |
| Serotype 33F (n=505, 499) | 49.5 | 1.6 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: GMC of Serotype-specific IgG 30 Days after Dose 2

| | |
|-----------------|---|
| End point title | GMC of Serotype-specific IgG 30 Days after Dose 2 |
|-----------------|---|

End point description:

The GMC of IgG serotype-specific antibodies to the 13 serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F) included in V114 and Prevenar 13™ and 2 serotypes (22F and 33F) unique to V114 were quantitated from participants' sera by a multiplex ECL assay. Immunoglobulin G for the 15 serotypes contained in V114 vaccine was determined using a PnECL assay. The analysis population for this endpoint included all randomized participants without protocol deviations that could have substantially impacted the results of the immunogenicity analyses and who had sufficient data to perform the analysis for each serotype.

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

End point timeframe:

30 days after Dose 2

| End point values | V114 | Prevenar 13™ | | |
|---|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 505 | 499 | | |
| Units: Geometric Mean Concentration (µg/mL) | | | | |
| number (not applicable) | | | | |
| Serotype 1 (n=505, 499) | 1.39 | 1.70 | | |
| Serotype 3 (n=505, 499) | 1.10 | 0.61 | | |
| Serotype 4 (n=505, 498) | 1.74 | 1.59 | | |
| Serotype 5 (n=505, 498) | 1.14 | 1.26 | | |
| Serotype 6A (n=505, 498) | 0.67 | 1.53 | | |
| Serotype 6B (n=505, 499) | 0.42 | 0.24 | | |
| Serotype 7F (n=505, 499) | 1.69 | 2.18 | | |
| Serotype 9V (n=504, 498) | 1.55 | 1.55 | | |
| Serotype 14 (n=504, 498) | 5.59 | 5.48 | | |
| Serotype 18C (n=505,499) | 1.18 | 1.58 | | |
| Serotype 19A (n=505, 499) | 1.70 | 2.35 | | |
| Serotype 19F (n=505, 499) | 2.79 | 4.04 | | |
| Serotype 23F (n=505, 498) | 0.71 | 0.54 | | |
| Serotype 22F (n=505, 499) | 3.16 | 0.04 | | |
| Serotype 33F (n=505, 499) | 0.30 | 0.04 | | |

Statistical analyses

| | |
|---|---------------------|
| Statistical analysis title | Serotype 1 |
| Comparison groups | V114 v Prevenar 13™ |
| Number of subjects included in analysis | 1004 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | GMC ratio |
| Point estimate | 0.82 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.75 |
| upper limit | 0.89 |

| | |
|---|---------------------|
| Statistical analysis title | Serotype 3 |
| Comparison groups | V114 v Prevenar 13™ |
| Number of subjects included in analysis | 1004 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | GMC ratio |
| Point estimate | 1.81 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.66 |
| upper limit | 1.98 |

| | |
|---|---------------------|
| Statistical analysis title | Serotype 4 |
| Comparison groups | V114 v Prevenar 13™ |
| Number of subjects included in analysis | 1004 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | GMC ratio |
| Point estimate | 1.09 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.99 |
| upper limit | 1.21 |

| | |
|-----------------------------------|---------------------|
| Statistical analysis title | Serotype 5 |
| Comparison groups | V114 v Prevenar 13™ |

| | |
|---|---------------|
| Number of subjects included in analysis | 1004 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | GMC ratio |
| Point estimate | 0.91 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.81 |
| upper limit | 1.01 |

| | |
|---|---------------------|
| Statistical analysis title | Serotype 6A |
| Comparison groups | V114 v Prevenar 13™ |
| Number of subjects included in analysis | 1004 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | GMC ratio |
| Point estimate | 0.44 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.38 |
| upper limit | 0.5 |

| | |
|---|---------------------|
| Statistical analysis title | Serotype 6B |
| Comparison groups | V114 v Prevenar 13™ |
| Number of subjects included in analysis | 1004 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | GMC ratio |
| Point estimate | 1.73 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.46 |
| upper limit | 2.05 |

| | |
|-----------------------------------|---------------------|
| Statistical analysis title | Serotype 7F |
| Comparison groups | V114 v Prevenar 13™ |

| | |
|---|---------------|
| Number of subjects included in analysis | 1004 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | GMC ratio |
| Point estimate | 0.78 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.71 |
| upper limit | 0.84 |

| | |
|---|---------------------|
| Statistical analysis title | Serotype 9V |
| Comparison groups | V114 v Prevenar 13™ |
| Number of subjects included in analysis | 1004 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | GMC ratio |
| Point estimate | 1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.9 |
| upper limit | 1.12 |

| | |
|---|---------------------|
| Statistical analysis title | Serotype 18C |
| Comparison groups | V114 v Prevenar 13™ |
| Number of subjects included in analysis | 1004 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | GMC ratio |
| Point estimate | 0.75 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.68 |
| upper limit | 0.82 |

| | |
|-----------------------------------|---------------------|
| Statistical analysis title | Serotype 14 |
| Comparison groups | V114 v Prevenar 13™ |

| | |
|---|---------------|
| Number of subjects included in analysis | 1004 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | GMC ratio |
| Point estimate | 1.02 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.89 |
| upper limit | 1.18 |

| | |
|---|---------------------|
| Statistical analysis title | Serotype 19A |
| Comparison groups | V114 v Prevenar 13™ |
| Number of subjects included in analysis | 1004 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | GMC ratio |
| Point estimate | 0.72 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.64 |
| upper limit | 0.81 |

| | |
|---|---------------------|
| Statistical analysis title | Serotype 19F |
| Comparison groups | V114 v Prevenar 13™ |
| Number of subjects included in analysis | 1004 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | GMC ratio |
| Point estimate | 0.69 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.62 |
| upper limit | 0.77 |

| | |
|-----------------------------------|---------------------|
| Statistical analysis title | Serotype 22F |
| Comparison groups | V114 v Prevenar 13™ |

| | |
|---|---------------|
| Number of subjects included in analysis | 1004 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| Parameter estimate | GMC ratio |
| Point estimate | 81.01 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 73.12 |
| upper limit | 89.75 |

| | |
|---|---------------------|
| Statistical analysis title | Serotype 23F |
| Comparison groups | V114 v Prevenar 13™ |
| Number of subjects included in analysis | 1004 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | GMC ratio |
| Point estimate | 1.32 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.16 |
| upper limit | 1.51 |

| | |
|---|---------------------|
| Statistical analysis title | Serotype 33F |
| Comparison groups | V114 v Prevenar 13™ |
| Number of subjects included in analysis | 1004 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | GMC ratio |
| Point estimate | 7.81 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 6.82 |
| upper limit | 8.94 |

Secondary: Percentage of Participants Meeting Specified Opsonophagocytic Activity (OPA) Responses 30 Days after Dose 3

| | |
|-----------------|---|
| End point title | Percentage of Participants Meeting Specified Opsonophagocytic Activity (OPA) Responses 30 Days after Dose 3 |
|-----------------|---|

End point description:

OPA for the 13 serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F) included in V114 and Prevenar 13™ and 2 serotypes unique to V114 (22F and 33F) was measured using a multiplex opsonophagocytic assay (MOPA). The analysis population for this endpoint included all randomized

participants in the OPA Subset without protocol deviations that could have substantially impacted the results of the immunogenicity analyses and who had sufficient data to perform the analysis for each serotype.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| 30 days after Dose 3 | |

| End point values | V114 | Prevenar 13™ | | |
|---|-----------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 108 | 95 | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| Serotype 1: % $\geq 1:9$ dilution (n=108, 94) | 98.1 (93.5 to 99.8) | 97.9 (92.5 to 99.7) | | |
| Serotype 3: % $\geq 1:19$ dilution (n=102, 92) | 99.0 (94.7 to 100.0) | 97.8 (92.4 to 99.7) | | |
| Serotype 4: % $\geq 1:34$ dilution (n=105, 92) | 100.0 (96.5 to 100.0) | 100.0 (96.1 to 100.0) | | |
| Serotype 5: % $\geq 1:27$ dilution (n=108, 95) | 100.0 (96.6 to 100.0) | 100.0 (96.2 to 100.0) | | |
| Serotype 6A: % $\geq 1:232$ dilution (n=100, 93) | 100.0 (96.4 to 100.0) | 100.0 (96.1 to 100.0) | | |
| Serotype 6B: % $\geq 1:40$ dilution (n=106, 93) | 100.0 (96.6 to 100.0) | 100.0 (96.1 to 100.0) | | |
| Serotype 7F: % $\geq 1:61$ dilution (n=106, 94) | 100.0 (96.6 to 100.0) | 100.0 (96.2 to 100.0) | | |
| Serotype 9V: % $\geq 1:151$ dilution (n=102, 91) | 99.0 (94.7 to 100.0) | 100.0 (96.0 to 100.0) | | |
| Serotype 14: % $\geq 1:62$ dilution (n=105, 93) | 100.0 (96.5 to 100.0) | 100.0 (96.1 to 100.0) | | |
| Serotype 18C: % $\geq 1:115$ dilution (n=104, 93) | 99.0 (94.8 to 100.0) | 100.0 (96.1 to 100.0) | | |
| Serotype 19A : % $\geq 1:31$ dilution (n=108, 93) | 100.0 (96.6 to 100.0) | 100.0 (96.1 to 100.0) | | |
| Serotype 19F: % $\geq 1:113$ dilution (n=104, 92) | 100.0 (96.5 to 100.0) | 100.0 (96.1 to 100.0) | | |
| Serotype 23F: % $\geq 1:55$ dilution (n=104, 91) | 100.0 (96.5 to 100.0) | 100.0 (96.0 to 100.0) | | |
| Serotype 22F: % $\geq 1:15$ dilution (n=104, 91) | 100.0 (96.5 to 100.0) | 26.4 (17.7 to 36.7) | | |
| Serotype 33F: % $\geq 1:20$ dilution (n=105, 95) | 100.0 (96.5 to 100.0) | 98.9 (94.3 to 100.0) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titers (GMTs) of Serotype-specific OPA 30 Days after Dose 3

| | |
|-----------------|--|
| End point title | Geometric Mean Titers (GMTs) of Serotype-specific OPA 30 Days after Dose 3 |
|-----------------|--|

End point description:

Sera from participants was used to measure GMT of the 13 serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F) included in V114 and Prevenar 13™ and 2 serotypes unique to V114 (22F and 33F) was determined using a MOPA. The analysis population for this endpoint included all randomized participants in the OPA Subset without protocol deviations that could have substantially impacted the results of the immunogenicity analyses and who had sufficient data to perform the analysis for each serotype.

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

End point timeframe:

30 days after Dose 3

| End point values | V114 | Prevenar 13™ | | |
|----------------------------------|------------------------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 108 | 95 | | |
| Units: GMT (1/dil) | | | | |
| number (confidence interval 95%) | | | | |
| Serotype 1 (n=108, 94) | 152.2 (122.6 to 189.0) | 184.0 (147.2 to 230.0) | | |
| Serotype 3 (n=102, 92) | 320.4 (266.9 to 384.8) | 296.2 (245.5 to 357.3) | | |
| Serotype 4 (n=105, 92) | 2290.8 (1856.9 to 2826.1) | 2842.0 (2404.6 to 3359.0) | | |
| Serotype 5 (n=108, 95) | 855.5 (699.9 to 1045.7) | 1024.5 (850.5 to 1234.0) | | |
| Serotype 6A (n=100, 93) | 3316.8 (2828.4 to 3889.5) | 4649.1 (3951.6 to 5469.7) | | |
| Serotype 6B (n=106, 93) | 2691.6 (2244.4 to 3227.8) | 2658.7 (2234.2 to 3163.8) | | |
| Serotype 7F (n=106, 94) | 5819.2 (4985.3 to 6792.7) | 7839.0 (6786.9 to 9054.2) | | |
| Serotype 9V (n=102, 91) | 2192.1 (1807.8 to 2658.1) | 2745.1 (2284.2 to 3298.9) | | |
| Serotype 14 (n=105, 93) | 3449.4 (2803.1 to 4244.7) | 2360.2 (1972.4 to 2824.3) | | |
| Serotype 18C (n=104, 93) | 2203.1 (1872.6 to 2592.1) | 2003.4 (1725.7 to 2325.7) | | |
| Serotype 19A (n=108, 93) | 2839.1 (2455.2 to 3282.9) | 3843.6 (3366.9 to 4387.8) | | |
| Serotype 19F (n=104, 92) | 1748.4 (1469.8 to 2079.7) | 2067.0 (1800.1 to 2373.4) | | |
| Serotype 23F (n= 104, 91) | 3650.2 (3041.3 to 4381.0) | 6776.2 (5344.0 to 8592.3) | | |
| Serotype 22F (n=104, 91) | 2927.9 (2547.0 to 3365.7) | 29.3 (17.8 to 48.4) | | |
| Serotype 33F (n=105, 95) | 13334.7 (11334.6 to 15687.7) | 1557.9 (1227.3 to 1977.5) | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Non-serious AEs: up to 14 days after each vaccination dose; serious AEs and deaths (all causes): up to approximately 6 months after Dose 3 (up to approximately 16 months)

Adverse event reporting additional description:

The safety analysis population included all randomized participants who received at least 1 dose of study vaccination. The analysis population for number of deaths (all causes) included all randomized participants.

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

Dictionary used

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

Reporting groups

| | |
|-----------------------|--------------|
| Reporting group title | Prevenar 13™ |
|-----------------------|--------------|

Reporting group description:

Participants received a single 0.5 mL IM injection of Prevenar 13™ at Visit 1, 2 and 4 (approximately 3, 5, and 12 months of age). As part of the study design, participants also received other pediatric vaccines, including Vaxelis™ (0.5 mL single dose at Visits 1, 2, and 4); M-M-R™II (0.5 mL single dose at Visit 4); and VARIVAX™ (0.5 mL single dose at Visit 4, except participants in Norway and Denmark, who received a second dose of VARIVAX™ at Visit 5, according to local vaccination requirements).

| | |
|-----------------------|------|
| Reporting group title | V114 |
|-----------------------|------|

Reporting group description:

Participants received a single 0.5 mL intramuscular (IM) injection of V114 at Visit 1, 2, and 4 (approximately 3, 5, and 12 months of age). As part of the study design, participants also received other pediatric vaccines, including Vaxelis™ (0.5 mL single dose at Visits 1, 2, and 4); M-M-R™II (0.5 mL single dose at Visit 4); and VARIVAX™ (0.5 mL single dose at Visit 4, except participants in Norway and Denmark, who received a second dose of VARIVAX™ at Visit 5, according to local vaccination requirements).

| Serious adverse events | Prevenar 13™ | V114 | |
|---|------------------|------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 28 / 594 (4.71%) | 30 / 595 (5.04%) | |
| number of deaths (all causes) | 0 | 1 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Brain neoplasm | | | |
| subjects affected / exposed | 0 / 594 (0.00%) | 1 / 595 (0.17%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Injury, poisoning and procedural complications | | | |
| Concussion | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 594 (0.17%) | 1 / 595 (0.17%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Post procedural haemorrhage | | | |
| subjects affected / exposed | 0 / 594 (0.00%) | 1 / 595 (0.17%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Congenital, familial and genetic disorders | | | |
| Laryngomalacia | | | |
| subjects affected / exposed | 0 / 594 (0.00%) | 1 / 595 (0.17%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Epilepsy | | | |
| subjects affected / exposed | 0 / 594 (0.00%) | 1 / 595 (0.17%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Febrile convulsion | | | |
| subjects affected / exposed | 1 / 594 (0.17%) | 0 / 595 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infantile spasms | | | |
| subjects affected / exposed | 0 / 594 (0.00%) | 1 / 595 (0.17%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Partial seizures | | | |
| subjects affected / exposed | 1 / 594 (0.17%) | 0 / 595 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Petit mal epilepsy | | | |
| subjects affected / exposed | 1 / 594 (0.17%) | 0 / 595 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|--|-----------------|-----------------|--|
| Tremor | | | |
| subjects affected / exposed | 0 / 594 (0.00%) | 1 / 595 (0.17%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 2 / 594 (0.34%) | 4 / 595 (0.67%) | |
| occurrences causally related to treatment / all | 1 / 2 | 2 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Immune system disorders | | | |
| Food allergy | | | |
| subjects affected / exposed | 0 / 594 (0.00%) | 1 / 595 (0.17%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 594 (0.17%) | 1 / 595 (0.17%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dysphagia | | | |
| subjects affected / exposed | 1 / 594 (0.17%) | 0 / 595 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Adenoidal hypertrophy | | | |
| subjects affected / exposed | 0 / 594 (0.00%) | 1 / 595 (0.17%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Tubulointerstitial nephritis | | | |
| subjects affected / exposed | 1 / 594 (0.17%) | 0 / 595 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |

| | | | |
|---|-----------------|-----------------|--|
| Muscular weakness | | | |
| subjects affected / exposed | 0 / 594 (0.00%) | 1 / 595 (0.17%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Arthritis infective | | | |
| subjects affected / exposed | 1 / 594 (0.17%) | 1 / 595 (0.17%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchiolitis | | | |
| subjects affected / exposed | 0 / 594 (0.00%) | 1 / 595 (0.17%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bacterial infection | | | |
| subjects affected / exposed | 0 / 594 (0.00%) | 1 / 595 (0.17%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchitis | | | |
| subjects affected / exposed | 1 / 594 (0.17%) | 2 / 595 (0.34%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cystitis | | | |
| subjects affected / exposed | 0 / 594 (0.00%) | 1 / 595 (0.17%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis | | | |
| subjects affected / exposed | 2 / 594 (0.34%) | 1 / 595 (0.17%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis adenovirus | | | |
| subjects affected / exposed | 1 / 594 (0.17%) | 0 / 595 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Laryngitis | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 3 / 594 (0.51%) | 1 / 595 (0.17%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pertussis | | | |
| subjects affected / exposed | 0 / 594 (0.00%) | 1 / 595 (0.17%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia respiratory syncytial viral | | | |
| subjects affected / exposed | 0 / 594 (0.00%) | 1 / 595 (0.17%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 594 (0.00%) | 1 / 595 (0.17%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyelonephritis | | | |
| subjects affected / exposed | 2 / 594 (0.34%) | 2 / 595 (0.34%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory syncytial virus bronchiolitis | | | |
| subjects affected / exposed | 3 / 594 (0.51%) | 1 / 595 (0.17%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory syncytial virus infection | | | |
| subjects affected / exposed | 1 / 594 (0.17%) | 1 / 595 (0.17%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory tract infection | | | |
| subjects affected / exposed | 1 / 594 (0.17%) | 0 / 595 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rhinitis | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 594 (0.17%) | 0 / 595 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory tract infection viral | | | |
| subjects affected / exposed | 1 / 594 (0.17%) | 0 / 595 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 594 (0.00%) | 1 / 595 (0.17%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Subcutaneous abscess | | | |
| subjects affected / exposed | 0 / 594 (0.00%) | 1 / 595 (0.17%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Viral infection | | | |
| subjects affected / exposed | 2 / 594 (0.34%) | 0 / 595 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 0 / 594 (0.00%) | 1 / 595 (0.17%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Type 1 diabetes mellitus | | | |
| subjects affected / exposed | 1 / 594 (0.17%) | 0 / 595 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | Prevenar 13™ | V114 | |
|---|--------------------|--------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 592 / 594 (99.66%) | 590 / 595 (99.16%) | |
| Investigations | | | |
| Body temperature increased | | | |
| subjects affected / exposed | 61 / 594 (10.27%) | 51 / 595 (8.57%) | |
| occurrences (all) | 91 | 74 | |
| Nervous system disorders | | | |
| Somnolence | | | |
| subjects affected / exposed | 463 / 594 (77.95%) | 460 / 595 (77.31%) | |
| occurrences (all) | 1085 | 1118 | |
| General disorders and administration site conditions | | | |
| Injection site pain | | | |
| subjects affected / exposed | 354 / 594 (59.60%) | 375 / 595 (63.03%) | |
| occurrences (all) | 595 | 646 | |
| Injection site induration | | | |
| subjects affected / exposed | 351 / 594 (59.09%) | 339 / 595 (56.97%) | |
| occurrences (all) | 679 | 658 | |
| Injection site erythema | | | |
| subjects affected / exposed | 389 / 594 (65.49%) | 357 / 595 (60.00%) | |
| occurrences (all) | 658 | 613 | |
| Injection site swelling | | | |
| subjects affected / exposed | 262 / 594 (44.11%) | 276 / 595 (46.39%) | |
| occurrences (all) | 417 | 444 | |
| Pyrexia | | | |
| subjects affected / exposed | 330 / 594 (55.56%) | 318 / 595 (53.45%) | |
| occurrences (all) | 762 | 728 | |
| Gastrointestinal disorders | | | |
| Vomiting | | | |
| subjects affected / exposed | 38 / 594 (6.40%) | 31 / 595 (5.21%) | |
| occurrences (all) | 41 | 38 | |
| Teething | | | |
| subjects affected / exposed | 50 / 594 (8.42%) | 47 / 595 (7.90%) | |
| occurrences (all) | 67 | 60 | |
| Diarrhoea | | | |
| subjects affected / exposed | 70 / 594 (11.78%) | 69 / 595 (11.60%) | |
| occurrences (all) | 89 | 82 | |

| | | | |
|--|----------------------------|----------------------------|--|
| Skin and subcutaneous tissue disorders Urticaria subjects affected / exposed occurrences (all) | 127 / 594 (21.38%) 173 | 100 / 595 (16.81%) 130 | |
| Psychiatric disorders Irritability subjects affected / exposed occurrences (all) | 559 / 594 (94.11%) 2304 | 573 / 595 (96.30%) 2266 | |
| Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) | 84 / 594 (14.14%) 101 | 70 / 595 (11.76%) 80 | |
| Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all) | 346 / 594 (58.25%) 686 | 326 / 595 (54.79%) 632 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-----------------|---|
| 14 October 2021 | Amendment 03: The primary purpose of this amendment was to expand the visit windows for Visit 2 (Dose 2 vaccination), Visit 3 (post-dose 2 blood draw), Visit 4 (Dose 3 vaccination), and Visit 5 (post-dose 3 blood draw) to allow inclusion of more participants in the immunogenicity analysis based on the per-protocol population. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported