# EU Clinical Trials Register

## Clinical trial results:
## Revaccination with Pneumococcal Conjugate Vaccine - Characterization of the Immune Response after Polysaccharide (REPLAY)

### Summary

| EudraCT number | 2008-006194-33 |
|---|---|
| Trial protocol | IS |
| Global end of trial date | 16 December 2009 |

### Results information

| Result version number | v1 (current) |
|---|---|
| This version publication date | 29 June 2016 |
| First version publication date | 17 July 2015 |

### Trial information

### Trial identification

| Sponsor protocol code | 6096A1-3013 |
|---|---|

### Additional study identifiers

| ISRCTN number | - |
|---|---|
| ClinicalTrials.gov id (NCT number) | NCT00853749 |
| WHO universal trial number (UTN) | - |
| Other trial identifiers | Alias: B1851012 |

Notes:

### Sponsors

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

Notes:

### Paediatric regulatory details

| Is trial part of an agreed paediatric investigation plan (PIP) | 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 November 2010 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 16 December 2009 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

To characterize the immune response by enzyme-linked immunosorbent assay (ELISA) and opsonophagocytic assay (OPA) at approximately one month after vaccination to a single dose of 13-valent pneumococcal conjugate vaccine (13vPnC) challenge in children vaccinated with a primary series (3 or 2 doses) of pneumococcal conjugate vaccine (PCV) followed by a booster dose of either PCV or 23-valent pneumococcal polysaccharide vaccine (23vPS).

Protection of trial subjects:

This study was conducted in compliance with the ethical principles originating in or derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. In addition, all local regulatory requirements were followed, in particular, those affording greater protection to the safety of trial subjects.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 05 May 2009 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Iceland: 89 |
| Worldwide total number of subjects | 89 |
| EEA total number of subjects | 89 |

Notes:

### Subjects enrolled per age group

| | |
|---|---|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 89 |
| 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:

Total 89 subjects were enrolled in a single site in Iceland. Study was started on 05 May 2009 and completed on 16 Dec 2009.

## Period 1

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

### Arms

| Are arms mutually exclusive? | Yes |
|---|---|
| **Arm title** | PCV/23vPS/13vPnC |

Arm description:

For this study, subjects received a single dose of 13vPnC. Subject previously must have also received an infant series of 9-valent pneumococcal-conjugate-meningococcal serogroup C conjugate combination vaccine (9V-MnCC) also known as PCV followed by a toddler dose of 23vPS.

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

Dosage and administration details:

Subjects received a single dose 0.5 milliliter (mL) 13vPnC.

| **Arm title** | PCV/PCV/13vPnC |
|---|---|

Arm description:

For this study, subjects received a single dose of 13vPnC. Subjects must have also previously received an infant series of 9V-MnCC followed by a toddler dose of 9V-MnCC (also referred to as PCV).

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

Dosage and administration details:

Subjects received a single dose of 0.5 mL 13vPnC.

| Number of subjects in period 1 | PCV/23vPS/13vPnC | PCV/PCV/13vPnC |
|---|---|---|
| Started | 50 | 39 |
| Vaccinated | 50 | 39 |
| Completed | 50 | 38 |
| Not completed | 0 | 1 |
|     Lost to follow-up | - | 1 |

## Baseline characteristics

### Reporting groups

| Reporting group title | PCV/23vPS/13vPnC |
|---|---|

Reporting group description:

For this study, subjects received a single dose of 13vPnC. Subject previously must have also received an infant series of 9-valent pneumococcal-conjugate-meningococcal serogroup C conjugate combination vaccine (9V-MnCC) also known as PCV followed by a toddler dose of 23vPS.

| Reporting group title | PCV/PCV/13vPnC |
|---|---|

Reporting group description:

For this study, subjects received a single dose of 13vPnC. Subjects must have also previously received an infant series of 9V-MnCC followed by a toddler dose of 9V-MnCC (also referred to as PCV).

| Reporting group values | PCV/23vPS/13vPnC | PCV/PCV/13vPnC | Total |
|---|---|---|---|
| Number of subjects | 50 | 39 | 89 |
| Age categorical | | | |
| Units: Subjects | | | |
| | | | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 7.6 | 7.6 | |
| standard deviation | ± 0.2 | ± 0.2 | - |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 25 | 20 | 45 |
| Male | 25 | 19 | 44 |

## End points

### End points reporting groups

| Reporting group title | PCV/23vPS/13vPnC |
|---|---|

Reporting group description:

For this study, subjects received a single dose of 13vPnC. Subject previously must have also received an infant series of 9-valent pneumococcal-conjugate-meningococcal serogroup C conjugate combination vaccine (9V-MnCC) also known as PCV followed by a toddler dose of 23vPS.

| Reporting group title | PCV/PCV/13vPnC |
|---|---|

Reporting group description:

For this study, subjects received a single dose of 13vPnC. Subjects must have also previously received an infant series of 9V-MnCC followed by a toddler dose of 9V-MnCC (also referred to as PCV).

### Primary: Percentage of Subjects Achieving a Predefined Serotype-specific Immunoglobulin G (IgG) Antibody Concentration Greater Than or Equal to ( ≥) 0.35 Micrograms Per Milliliter (Mcg/mL) Measured 1 Month After Vaccination

| End point title | Percentage of Subjects Achieving a Predefined Serotype-specific Immunoglobulin G (IgG) Antibody Concentration Greater Than or Equal to ( ≥) 0.35 Micrograms Per Milliliter (Mcg/mL) Measured 1 Month After Vaccination |
|---|---|

End point description:

Percentage of subjects achieving predefined antibody threshold ≥ 0.35 mcg/mL along with the corresponding 95 percent (%) Confidence Interval (CI) for the 7 common pneumococcal serotypes (serotypes 4, 6B, 9V, 14, 18C, 19F, and 23F) and 6 additional pneumococcal serotypes specific to 13vPnC (serotypes 1, 3, 5, 6A, 7F, and 19A) are presented. Exact 2-sided CI based on the observed proportion of subjects. Evaluable Immunogenicity Population: received 1 dose of 13vPnC at Visit 1, blood drawn within specified timeframes, at least 1 valid and determinate assay result at Visits 1 and 3, no major protocol violations, and no prohibited vaccines.

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

End point timeframe:

Day 28

| End point values | PCV/23vPS/13vPnC | PCV/PCV/13vPnC | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 50[1] | 37[2] | | |
| Units: percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| Common Serotype 4 | 100 (92.9 to 100) | 97.3 (85.8 to 99.9) | | |
| Common Serotype 6B | 100 (92.9 to 100) | 100 (90.5 to 100) | | |
| Common Serotype 9V | 100 (92.9 to 100) | 100 (90.5 to 100) | | |
| Common Serotype 14 | 100 (92.7 to 100) | 100 (90.5 to 100) | | |
| Common Serotype18C | 100 (92.9 to 100) | 97.3 (85.8 to 99.9) | | |
| Common Serotype 19F | 100 (92.9 to 100) | 100 (90.5 to 100) | | |

| | | | | |
|---|---|---|---|---|
| Common Serotype 23F | 100 (92.9 to 100) | 100 (90.5 to 100) | | |
| Additional Serotype 1 | 100 (92.9 to 100) | 97.3 (85.8 to 99.9) | | |
| Additional Serotype 3 | 100 (92.9 to 100) | 100 (90.5 to 100) | | |
| Additional Serotype 5 | 100 (92.9 to 100) | 100 (90.5 to 100) | | |
| Additional Serotype 6A | 100 (92.9 to 100) | 100 (90.5 to 100) | | |
| Additional Serotype 7F | 100 (92.9 to 100) | 100 (90.5 to 100) | | |
| Additional Serotype 19A | 100 (92.9 to 100) | 100 (90.5 to 100) | | |

Notes:

[1] - N= Number of subjects with a determinate IgG antibody concentration to the given serotype.

[2] - N= Number of subjects with a determinate IgG antibody concentration to the given serotype.

## Statistical analyses

| Statistical analysis title | Comparison for Common Serotype 4 |
|---|---|
| Comparison groups | PCV/23vPS/13vPnC v PCV/PCV/13vPnC |
| Number of subjects included in analysis | 87 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | Difference in proportions (percentage) |
| Point estimate | 2.7 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -5 |
| upper limit | 14.2 |

| Statistical analysis title | Comparison for Common Serotype 6B |
|---|---|
| Comparison groups | PCV/23vPS/13vPnC v PCV/PCV/13vPnC |
| Number of subjects included in analysis | 87 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | Difference in proportions (percentage) |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -7.3 |
| upper limit | 9.5 |

| Statistical analysis title | Comparison for Common Serotype 9V |
|---|---|
| Comparison groups | PCV/23vPS/13vPnC v PCV/PCV/13vPnC |

| | |
|---|---|
| Number of subjects included in analysis | 87 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | Difference in proportions (percentage) |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -7.3 |
| upper limit | 9.5 |

| **Statistical analysis title** | Comparison for Common Serotype 14 |
|---|---|
| Comparison groups | PCV/23vPS/13vPnC v PCV/PCV/13vPnC |
| Number of subjects included in analysis | 87 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | Difference in proportions (percentage) |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -7.8 |
| upper limit | 9.5 |

| **Statistical analysis title** | Comparison for Common Serotype 18C |
|---|---|
| Comparison groups | PCV/23vPS/13vPnC v PCV/PCV/13vPnC |
| Number of subjects included in analysis | 87 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | Difference in proportions (percentage) |
| Point estimate | 2.7 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -5 |
| upper limit | 14.2 |

| **Statistical analysis title** | Comparison for Common Serotype 19F |
|---|---|
| Comparison groups | PCV/23vPS/13vPnC v PCV/PCV/13vPnC |

| | |
|---|---|
| Number of subjects included in analysis | 87 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | Difference in proportions (percentage) |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -7.3 |
| upper limit | 9.5 |

| | |
|---|---|
| **Statistical analysis title** | Comparison for Common Serotype 23F |
| Comparison groups | PCV/23vPS/13vPnC v PCV/PCV/13vPnC |
| Number of subjects included in analysis | 87 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | Difference in proportions (percentage) |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -7.3 |
| upper limit | 9.5 |

| | |
|---|---|
| **Statistical analysis title** | Comparison for Additional Serotype 1 |
| Comparison groups | PCV/23vPS/13vPnC v PCV/PCV/13vPnC |
| Number of subjects included in analysis | 87 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | Difference in proportions (percentage) |
| Point estimate | 2.7 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -5 |
| upper limit | 14.2 |

| | |
|---|---|
| **Statistical analysis title** | Comparison for Additional Serotype 3 |
| Comparison groups | PCV/23vPS/13vPnC v PCV/PCV/13vPnC |

| | |
|---|---|
| Number of subjects included in analysis | 87 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | Difference in proportions (percentage) |
| Point estimate | 0 |
| Confidence interval | |
|     level | 95 % |
|     sides | 2-sided |
|     lower limit | -7.3 |
|     upper limit | 9.5 |

| | |
|---|---|
| **Statistical analysis title** | Comparison for Additional Serotype 5 |
| Comparison groups | PCV/23vPS/13vPnC v PCV/PCV/13vPnC |
| Number of subjects included in analysis | 87 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | Difference in proportions (percentage) |
| Point estimate | 0 |
| Confidence interval | |
|     level | 95 % |
|     sides | 2-sided |
|     lower limit | -7.3 |
|     upper limit | 9.5 |

| | |
|---|---|
| **Statistical analysis title** | Comparison for Additional Serotype 6A |
| Comparison groups | PCV/23vPS/13vPnC v PCV/PCV/13vPnC |
| Number of subjects included in analysis | 87 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | Difference in proportions (percentage) |
| Point estimate | 0 |
| Confidence interval | |
|     level | 95 % |
|     sides | 2-sided |
|     lower limit | -7.3 |
|     upper limit | 9.5 |

| | |
|---|---|
| **Statistical analysis title** | Comparison for Additional Serotype 7F |
| Comparison groups | PCV/23vPS/13vPnC v PCV/PCV/13vPnC |

| Number of subjects included in analysis | 87 |
|---|---|
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | Difference in proportions (percentage) |
| Point estimate | 0 |
| Confidence interval | |
|     level | 95 % |
|     sides | 2-sided |
|     lower limit | -7.3 |
|     upper limit | 9.5 |

| **Statistical analysis title** | Comparison for Additional Serotype 19A |
|---|---|
| Comparison groups | PCV/23vPS/13vPnC v PCV/PCV/13vPnC |
| Number of subjects included in analysis | 87 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | Difference in proportions (percentage) |
| Point estimate | 0 |
| Confidence interval | |
|     level | 95 % |
|     sides | 2-sided |
|     lower limit | -7.3 |
|     upper limit | 9.5 |

**Primary: Percentage of Subjects Achieving Opsonophagocytic Assay (OPA) Titers ≥ 1:8 Measured 1 Month After Vaccination**

| End point title | Percentage of Subjects Achieving Opsonophagocytic Assay (OPA) Titers ≥ 1:8 Measured 1 Month After Vaccination |
|---|---|

End point description:

Percentage of subjects achieving OPA along with the corresponding 95% CI for the 7 common pneumococcal serotypes (serotypes 4, 6B, 9V, 14, 18C, 19F, and 23F) and 6 additional pneumococcal serotypes specific to 13vPnC (serotypes 1, 3, 5, 6A, 7F, and 19A) are presented. Exact 2-sided CI based on the observed proportion of subjects. Evaluable immunogenicity population.

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

End point timeframe:

Day 28

| **End point values** | PCV/23vPS/13vPnC | PCV/PCV/13vPnC | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 50[3] | 37[4] | | |
| Units: percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
|     Common Serotype 4 | 98 (89.4 to 99.9) | 97.2 (85.5 to 99.9) | | |

| | | | | |
|---|---|---|---|---|
| Common Serotype 6B | 100 (92.7 to 100) | 100 (90.3 to 100) | | |
| Common Serotype 9V | 100 (92.7 to 100) | 100 (90.3 to 100) | | |
| Common Serotype 14 | 100 (92.7 to 100) | 100 (90.3 to 100) | | |
| Common Serotype 18C | 100 (92.9 to 100) | 100 (90 to 100) | | |
| Common Serotype 19F | 100 (92.7 to 100) | 100 (90 to 100) | | |
| Common Serotype 23F | 98 (89.4 to 99.9) | 100 (89.7 to 100) | | |
| Additional Serotype 1 | 100 (92.9 to 100) | 97.3 (85.8 to 99.9) | | |
| Additional Serotype 3 | 98 (89.1 to 99.9) | 100 (90.3 to 100) | | |
| Additional Serotype 5 | 98 (89.4 to 99.9) | 97.3 (85.8 to 99.9) | | |
| Additional Serotype 6A | 100 (92.9 to 100) | 100 (90.5 to 100) | | |
| Additional Serotype 7F | 98 (89.4 to 99.9) | 100 (90.3 to 100) | | |
| Additional Serotype 19A | 100 (92.9 to 100) | 100 (90.5 to 100) | | |

Notes:

[3] - N=number of subjects with a determinate OPA antibody titer to the given serotype.

[4] - N=number of subjects with a determinate OPA antibody titer to the given serotype.

## Statistical analyses

| **Statistical analysis title** | Comparison for Common Serotype 4 |
|---|---|
| Comparison groups | PCV/23vPS/13vPnC v PCV/PCV/13vPnC |
| Number of subjects included in analysis | 87 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | Difference in proportions (percentage) |
| Point estimate | 0.8 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -8.6 |
| upper limit | 12.7 |

| **Statistical analysis title** | Comparison for Common Serotype 6B |
|---|---|
| Comparison groups | PCV/23vPS/13vPnC v PCV/PCV/13vPnC |
| Number of subjects included in analysis | 87 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | Difference in proportions (percentage) |
| Point estimate | 0 |

| Confidence interval | |
| --- | --- |
| level | 95 % |
| sides | 2-sided |
| lower limit | -7.5 |
| upper limit | 9.7 |

| **Statistical analysis title** | Comparison for Common Serotype 9V |
| --- | --- |
| Comparison groups | PCV/23vPS/13vPnC v PCV/PCV/13vPnC |
| Number of subjects included in analysis | 87 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | Difference in proportions (percentage) |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -7.5 |
| upper limit | 9.7 |

| **Statistical analysis title** | Comparison for Common Serotype 14 |
| --- | --- |
| Comparison groups | PCV/23vPS/13vPnC v PCV/PCV/13vPnC |
| Number of subjects included in analysis | 87 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | Difference in proportions (percentage) |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -7.5 |
| upper limit | 9.7 |

| **Statistical analysis title** | Comparison for Common Serotype 18C |
| --- | --- |
| Comparison groups | PCV/23vPS/13vPnC v PCV/PCV/13vPnC |
| Number of subjects included in analysis | 87 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | Difference in proportions (percentage) |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -7.4 |
| upper limit | 10 |

| Statistical analysis title | Comparison for Common Serotype 19F |
|---|---|
| Comparison groups | PCV/23vPS/13vPnC v PCV/PCV/13vPnC |
| Number of subjects included in analysis | 87 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | Difference in proportions (percentage) |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -7.5 |
| upper limit | 10 |

| Statistical analysis title | Comparison for Common Serotype 23F |
|---|---|
| Comparison groups | PCV/23vPS/13vPnC v PCV/PCV/13vPnC |
| Number of subjects included in analysis | 87 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | Difference in proportions (percentage) |
| Point estimate | -2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -10.8 |
| upper limit | 8.1 |

| Statistical analysis title | Comparison for Additional Serotype 1 |
|---|---|
| Comparison groups | PCV/23vPS/13vPnC v PCV/PCV/13vPnC |
| Number of subjects included in analysis | 87 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | Difference in proportions (percentage) |
| Point estimate | 2.7 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -5 |
| upper limit | 14.2 |

| Statistical analysis title | Comparison for Additional Serotype 3 |
|---|---|

| Comparison groups | PCV/23vPS/13vPnC v PCV/PCV/13vPnC |
|---|---|
| Number of subjects included in analysis | 87 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate |  Difference in proportions (percentage) |
| Point estimate | -2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -11.1 |
| upper limit | 7.9 |

| Statistical analysis title | Comparison for Additional Serotype 5 |
|---|---|
| Comparison groups | PCV/23vPS/13vPnC v PCV/PCV/13vPnC |
| Number of subjects included in analysis | 87 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate |  Difference in proportions (percentage) |
| Point estimate | 0.7 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -8.5 |
| upper limit | 12.2 |

| Statistical analysis title | Comparison for Additional Serotype 6A |
|---|---|
| Comparison groups | PCV/23vPS/13vPnC v PCV/PCV/13vPnC |
| Number of subjects included in analysis | 87 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate |  Difference in proportions (percentage) |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -7.3 |
| upper limit | 9.5 |

| Statistical analysis title | Comparison for Additional Serotype 7F |
|---|---|
| Comparison groups | PCV/23vPS/13vPnC v PCV/PCV/13vPnC |

| | |
|---|---|
| Number of subjects included in analysis | 87 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | Difference in proportions (percentage) |
| Point estimate | -2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -11.3 |
| upper limit | 7.7 |

| | |
|---|---|
| **Statistical analysis title** | Comparison for Additional Serotype 19A |
| Comparison groups | PCV/23vPS/13vPnC v PCV/PCV/13vPnC |
| Number of subjects included in analysis | 87 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | Difference in proportions (percentage) |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -7.3 |
| upper limit | 9.5 |

## Secondary: Antibody Response Measured 1 Month After Vaccination (Avidity Assay)

| | |
|---|---|
| End point title | Antibody Response Measured 1 Month After Vaccination (Avidity Assay) |

End point description:

Avidity assay had measurable range of 0.117 to 7.5. Results expressed as Avidity Index (AI). Geometric mean avidity presented for 3 common pneumococcal serotypes (serotype 6B, 19F, and 23F) and 2 additional pneumococcal serotypes specific to 13vPnC (Serotypes 1 and 5). Evaluable imunogenicity population; in accordance with the recommendation of the lab completing the assays, values above the upper limit were assigned a value of 8.0 and those below the lower limit were assigned a value of 0.10.

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

End point timeframe:

Day 28

| **End point values** | PCV/23vPS/13vPnC | PCV/PCV/13vPnC | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 50[5] | 36[6] | | |
| Units: AI | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Additional serotype 1 | 1.42 (1.15 to 1.76) | 4.68 (3.62 to 6.04) | | |

| | | | | |
|---|---|---|---|---|
| Additional serotype 5 | 1.85 (1.46 to 2.36) | 5.85 (4.81 to 7.11) | | |
| Common serotype 6B | 2.43 (1.77 to 3.35) | 5.48 (4.38 to 6.86) | | |
| Common serotype 19F | 2.17 (1.69 to 2.79) | 2.46 (1.88 to 3.21) | | |
| Common serotype 23F | 3.02 (2.36 to 3.85) | 6.43 (5.33 to 7.76) | | |

Notes:

[5] - N=number of subjects with a determinate avidity index for the specified serotype.

[6] - N=number of subjects with a determinate avidity index for the specified serotype.

## Statistical analyses

| **Statistical analysis title** | Serotype 1 |
|---|---|
| Statistical analysis description: | |
| Confidence Intervals (CIs) for the ratio were back transformations of a CI based on the Student t distribution for the mean difference of the logarithms of the measures (PCV/23vPS/13vPnC, PCV/PCV/13vPnC). | |
| Comparison groups | PCV/23vPS/13vPnC v PCV/PCV/13vPnC |
| Number of subjects included in analysis | 86 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | Ratio of geometric means |
| Point estimate | 0.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.22 |
| upper limit | 0.42 |

| **Statistical analysis title** | Serotype 5 |
|---|---|
| Statistical analysis description: | |
| CIs for the ratio were back transformations of a CI based on the Student t distribution for the mean difference of the logarithms of the measures (PCV/23vPS/13vPnC, PCV/PCV/13vPnC). | |
| Comparison groups | PCV/23vPS/13vPnC v PCV/PCV/13vPnC |
| Number of subjects included in analysis | 86 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | Ratio of geometric means |
| Point estimate | 0.32 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.23 |
| upper limit | 0.44 |

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

Statistical analysis description:

CIs for the ratio were back transformations of a CI based on the Student t distribution for the mean difference of the logarithms of the measures (PCV/23vPS/13vPnC, PCV/PCV/13vPnC).

| Comparison groups | PCV/23vPS/13vPnC v PCV/PCV/13vPnC |
|---|---|
| Number of subjects included in analysis | 86 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | Ratio of geometric means |
| Point estimate | 0.44 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.29 |
| upper limit | 0.67 |

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

Statistical analysis description:

CIs for the ratio were back transformations of a CI based on the Student t distribution for the mean difference of the logarithms of the measures (PCV/23vPS/13vPnC, PCV/PCV/13vPnC).

| Comparison groups | PCV/23vPS/13vPnC v PCV/PCV/13vPnC |
|---|---|
| Number of subjects included in analysis | 86 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | Ratio of geometric means |
| Point estimate | 0.88 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.61 |
| upper limit | 1.27 |

| **Statistical analysis title** | Serotype 23F |
|---|---|

Statistical analysis description:

CIs for the ratio were back transformations of a CI based on the Student t distribution for the mean difference of the logarithms of the measures (PCV/23vPS/13vPnC, PCV/PCV/13vPnC).

| Comparison groups | PCV/23vPS/13vPnC v PCV/PCV/13vPnC |
|---|---|
| Number of subjects included in analysis | 86 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | Ratio of geometric means |
| Point estimate | 0.47 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.34 |
| upper limit | 0.65 |

## Secondary: Antibody Response Measured 1 Month After Vaccination (OPA)

| End point title | Antibody Response Measured 1 Month After Vaccination (OPA) |
|---|---|
| End point description: | |

Antibody response as measured by OPA, 1 month after vaccination. Geometric mean titers (GMTs) calculated using all subjects with available data for the specified blood draw. CIs were back transformations of a CI based on the Student t distribution for the mean logarithm of the titers. Evaluable immunogenicity population.

| End point type | Secondary |
|---|---|
| End point timeframe: | |

Day 28

| End point values | PCV/23vPS/13 vPnC | PCV/PCV/13vP nC | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 50[7] | 37[8] | | |
| Units: GMT | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Common Serotype 4 | 2374 (1656.3 to 3404) | 3765 (2339.1 to 6059.8) | | |
| Common Serotype 6B | 11156 (9073.5 to 13715.2) | 11477 (8418.5 to 15646.8) | | |
| Common Serotype 9V | 1651 (1067.8 to 2553.3) | 1713 (1087 to 2700) | | |
| Common Serotype 14 | 3041 (2311.4 to 4001.1) | 3048 (2318.3 to 4006.9) | | |
| Common Serotype 18C | 3230 (2616.1 to 3987.1) | 5684 (3122.2 to 10349.6) | | |
| Common Serotype 19F | 1266 (1013.9 to 1582) | 1198 (842.3 to 1703.9) | | |
| Common Serotype 23F | 1678 (1212.3 to 2322.1) | 2714 (1970.1 to 3739.5) | | |
| Additional Serotype 1 | 217 (162.6 to 290.5) | 1087 (717.5 to 1646.3) | | |
| Additional Serotype 3 | 153 (117.2 to 200.2) | 188 (146.6 to 240.8) | | |
| Additional Serotype 5 | 264 (178.5 to 389.9) | 719 (500.9 to 1032.4) | | |
| Additional Serotype 6A | 7060 (5352.2 to 9312.6) | 5034 (3336.6 to 7594.4) | | |
| Additional Serotype 7F | 5835 (4160 to 8184.1) | 7887 (6447.9 to 9647) | | |
| Additional Serotype 19A | 1256 (990.9 to 1591.9) | 1556 (1108.8 to 2182.2) | | |

Notes:

[7] - N=number of subjects with a determinate antibody titre to the specified serotype.

[8] - N=number of subjects with a determinate antibody titre to the specified serotype.

## Statistical analyses

| Statistical analysis title | Common Serotype 4 |
|---|---|

Statistical analysis description:

Ratio of GMTs (PCV/23vPS/13vPnC, PCV/PCV/13vPnC). CIs for the ratio were back transformations of a CI based on the Student t distribution for the mean difference of the logarithms of the measures (PCV/23vPS/13vPnC, PCV/PCV/13vPnC).

| Comparison groups | PCV/23vPS/13vPnC v PCV/PCV/13vPnC |
|---|---|
| Number of subjects included in analysis | 87 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | Ratio of GMTs |
| Point estimate | 0.6 |
| Confidence interval | |
|     level | 95 % |
|     sides | 2-sided |
|     lower limit | 0.35 |
|     upper limit | 1.12 |

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

Statistical analysis description:

Ratio of GMTs (PCV/23vPS/13vPnC, PCV/PCV/13vPnC). CIs for the ratio were back transformations of a CI based on the Student t distribution for the mean difference of the logarithms of the measures (PCV/23vPS/13vPnC, PCV/PCV/13vPnC).

| Comparison groups | PCV/PCV/13vPnC v PCV/23vPS/13vPnC |
|---|---|
| Number of subjects included in analysis | 87 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | Ratio of GMTs |
| Point estimate | 1 |
| Confidence interval | |
|     level | 95 % |
|     sides | 2-sided |
|     lower limit | 0.68 |
|     upper limit | 1.38 |

| Statistical analysis title | Common Serotype 9V |
|---|---|

Statistical analysis description:

Ratio of GMTs (PCV/23vPS/13vPnC, PCV/PCV/13vPnC). CIs for the ratio were back transformations of a CI based on the Student t distribution for the mean difference of the logarithms of the measures (PCV/23vPS/13vPnC, PCV/PCV/13vPnC).

| Comparison groups | PCV/23vPS/13vPnC v PCV/PCV/13vPnC |
|---|---|
| Number of subjects included in analysis | 87 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | Ratio of GMTs |
| Point estimate | 1 |

| Confidence interval | |
|---|---|
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.51 |
| upper limit | 1.81 |

| **Statistical analysis title** | Common Serotype 14 |
|---|---|

Statistical analysis description:

Ratio of GMTs (PCV/23vPS/13vPnC, PCV/PCV/13vPnC). CIs for the ratio were back transformations of a CI based on the Student t distribution for the mean difference of the logarithms of the measures (PCV/23vPS/13vPnC, PCV/PCV/13vPnC).

| Comparison groups | PCV/23vPS/13vPnC v PCV/PCV/13vPnC |
|---|---|
| Number of subjects included in analysis | 87 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | Ratio of GMTs |
| Point estimate | 1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.67 |
| upper limit | 1.48 |

| **Statistical analysis title** | Common Serotype 18C |
|---|---|

Statistical analysis description:

Ratio of GMTs (PCV/23vPS/13vPnC, PCV/PCV/13vPnC). CIs for the ratio were back transformations of a CI based on the Student t distribution for the mean difference of the logarithms of the measures (PCV/23vPS/13vPnC, PCV/PCV/13vPnC).

| Comparison groups | PCV/23vPS/13vPnC v PCV/PCV/13vPnC |
|---|---|
| Number of subjects included in analysis | 87 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | Ratio of GMTs |
| Point estimate | 0.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.33 |
| upper limit | 0.98 |

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

Statistical analysis description:

Ratio of GMTs (PCV/23vPS/13vPnC, PCV/PCV/13vPnC). CIs for the ratio were back transformations of a CI based on the Student t distribution for the mean difference of the logarithms of the measures (PCV/23vPS/13vPnC, PCV/PCV/13vPnC).

| Comparison groups | PCV/23vPS/13vPnC v PCV/PCV/13vPnC |
|---|---|
| Number of subjects included in analysis | 87 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | Ratio of GMTs |
| Point estimate | 1.1 |
| Confidence interval | |
|     level | 95 % |
|     sides | 2-sided |
|     lower limit | 0.72 |
|     upper limit | 1.56 |

| **Statistical analysis title** | Common Serotype 23F |
|---|---|

Statistical analysis description:

Ratio of GMTs (PCV/23vPS/13vPnC, PCV/PCV/13vPnC). CIs for the ratio were back transformations of a CI based on the Student t distribution for the mean difference of the logarithms of the measures (PCV/23vPS/13vPnC, PCV/PCV/13vPnC).

| Comparison groups | PCV/23vPS/13vPnC v PCV/PCV/13vPnC |
|---|---|
| Number of subjects included in analysis | 87 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | Ratio of GMTs |
| Point estimate | 0.6 |
| Confidence interval | |
|     level | 95 % |
|     sides | 2-sided |
|     lower limit | 0.39 |
|     upper limit | 0.99 |

| **Statistical analysis title** | Additional Serotype 1 |
|---|---|

Statistical analysis description:

Ratio of GMTs (PCV/23vPS/13vPnC, PCV/PCV/13vPnC). CIs for the ratio were back transformations of a CI based on the Student t distribution for the mean difference of the logarithms of the measures (PCV/23vPS/13vPnC, PCV/PCV/13vPnC).

| Comparison groups | PCV/23vPS/13vPnC v PCV/PCV/13vPnC |
|---|---|
| Number of subjects included in analysis | 87 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | Ratio of GMTs |
| Point estimate | 0.2 |
| Confidence interval | |
|     level | 95 % |
|     sides | 2-sided |
|     lower limit | 0.12 |
|     upper limit | 0.32 |

| **Statistical analysis title** | Additional Serotype 3 |
|---|---|

Statistical analysis description:

Ratio of GMTs (PCV/23vPS/13vPnC, PCV/PCV/13vPnC). CIs for the ratio were back transformations of a CI based on the Student t distribution for the mean difference of the logarithms of the measures (PCV/23vPS/13vPnC, PCV/PCV/13vPnC).

| Comparison groups | PCV/23vPS/13vPnC v PCV/PCV/13vPnC |
|---|---|
| Number of subjects included in analysis | 87 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | Ratio of GMTs |
| Point estimate | 0.8 |
| Confidence interval | |
|     level | 95 % |
|     sides | 2-sided |
|     lower limit | 0.56 |
|     upper limit | 1.18 |

| **Statistical analysis title** | Additional Serotype 5 |
|---|---|

Statistical analysis description:

Ratio of GMTs (PCV/23vPS/13vPnC, PCV/PCV/13vPnC). CIs for the ratio were back transformations of a CI based on the Student t distribution for the mean difference of the logarithms of the measures (PCV/23vPS/13vPnC, PCV/PCV/13vPnC).

| Comparison groups | PCV/23vPS/13vPnC v PCV/PCV/13vPnC |
|---|---|
| Number of subjects included in analysis | 87 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | Ratio of GMTs |
| Point estimate | 0.4 |
| Confidence interval | |
|     level | 95 % |
|     sides | 2-sided |
|     lower limit | 0.21 |
|     upper limit | 0.63 |

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

Statistical analysis description:

Ratio of GMTs (PCV/23vPS/13vPnC, PCV/PCV/13vPnC). CIs for the ratio were back transformations of a CI based on the Student t distribution for the mean difference of the logarithms of the measures (PCV/23vPS/13vPnC, PCV/PCV/13vPnC).

| Comparison groups | PCV/PCV/13vPnC v PCV/23vPS/13vPnC |
|---|---|

| | |
|---|---|
| Number of subjects included in analysis | 87 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | Ratio of GMTs |
| Point estimate | 1.4 |
| Confidence interval | |
|     level | 95 % |
|     sides | 2-sided |
|     lower limit | 0.88 |
|     upper limit | 2.25 |

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

Statistical analysis description:

Ratio of GMTs (PCV/23vPS/13vPnC, PCV/PCV/13vPnC). CIs for the ratio were back transformations of a CI based on the Student t distribution for the mean difference of the logarithms of the measures (PCV/23vPS/13vPnC, PCV/PCV/13vPnC).

| | |
|---|---|
| Comparison groups | PCV/23vPS/13vPnC v PCV/PCV/13vPnC |
| Number of subjects included in analysis | 87 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | Ratio of GMTs |
| Point estimate | 0.7 |
| Confidence interval | |
|     level | 95 % |
|     sides | 2-sided |
|     lower limit | 0.48 |
|     upper limit | 1.14 |

| | |
|---|---|
| **Statistical analysis title** | Additional Serotype 19A |

Statistical analysis description:

Ratio of GMTs (PCV/23vPS/13vPnC, PCV/PCV/13vPnC). CIs for the ratio were back transformations of a CI based on the Student t distribution for the mean difference of the logarithms of the measures (PCV/23vPS/13vPnC, PCV/PCV/13vPnC).

| | |
|---|---|
| Comparison groups | PCV/23vPS/13vPnC v PCV/PCV/13vPnC |
| Number of subjects included in analysis | 87 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | Ratio of GMTs |
| Point estimate | 0.8 |
| Confidence interval | |
|     level | 95 % |
|     sides | 2-sided |
|     lower limit | 0.54 |
|     upper limit | 1.2 |

## Other pre-specified: Geometric Mean Concentration (GMC) for Serotype-specific Pneumococcal IgG Antibody 1 Month After Vaccination

| End point title | Geometric Mean Concentration (GMC) for Serotype-specific Pneumococcal IgG Antibody 1 Month After Vaccination |
|---|---|

End point description:

Antibody GMC as measured by mcg/mL for 7 common pneumococcal serotypes (serotypes 4, 6B, 9V, 14, 18C, 19F, and 23F) and 6 additional pneumococcal serotypes specific to 13vPnC (Serotypes 1, 3, 5, 6A, 7F, and 19A) are presented. GMC (13vPnC) and corresponding 2-sided 95% CIs were evaluated. CIs were back transformations of a CI based on the Student t distribution for the mean logarithm of the concentrations. GMCs were calculated using all subjects with available data for the specified blood draw. Evaluable Immunogenicity Population.

| End point type | Other pre-specified |
|---|---|

End point timeframe:

Day 28

| End point values | PCV/23vPS/13vPnC | PCV/PCV/13vPnC | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 50[9] | 37[10] | | |
| Units: mcg/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Common serotype 4 | 4.18 (3.38 to 5.16) | 11.34 (7.74 to 16.62) | | |
| Common serotype 6B | 29.51 (21.32 to 40.83) | 41.7 (29.01 to 59.96) | | |
| Common serotype 9V | 4.31 (3.68 to 5.04) | 7.39 (6.05 to 9.03) | | |
| Common serotype 14 | 17.47 (12.76 to 23.93) | 22.78 (15.75 to 32.96) | | |
| Common serotype 18C | 2.76 (2.15 to 3.56) | 4.83 (3.48 to 6.71) | | |
| Common serotype 19F | 9.78 (7.45 to 12.83) | 11.6 (8.46 to 15.92) | | |
| Common serotype 23F | 7.89 (6.18 to 10.07) | 12.25 (8.92 to 16.81) | | |
| Additional serotype 1 | 5.28 (4.22 to 6.61) | 19.43 (13.77 to 27.41) | | |
| Additional serotype 3 | 3.28 (2.44 to 4.41) | 2.87 (2.19 to 3.76) | | |
| Additional serotype 5 | 5.75 (4.64 to 7.12) | 15.98 (11.99 to 21.3) | | |
| Additional serotype 6A | 11.16 (8.8 to 14.16) | 14.07 (10.64 to 18.61) | | |
| Additional serotype 7F | 7.13 (5.67 to 8.96) | 8.05 (5.94 to 10.91) | | |
| Additional serotype 19A | 14.62 (11.49 to 18.59) | 17.07 (12.92 to 22.55) | | |

Notes:

[9] - N=number of subjects with a determinate antibody concentration to the specified serotype.

[10] - N=number of subjects with a determinate antibody concentration to the specified serotype.

## Statistical analyses

| Statistical analysis title | Common Serotype 4 |
|---|---|

Statistical analysis description:

Ratio of GMCs (PCV/23vPS/13vPnC, PCV/PCV/13vPnC). CIs for the ratio were back transformations of a CI based on the Student t distribution for the mean difference of the logarithms of the measures (PCV/23vPS/13vPnC, PCV/PCV/13vPnC).

| Comparison groups | PCV/23vPS/13vPnC v PCV/PCV/13vPnC |
|---|---|
| Number of subjects included in analysis | 87 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | Ratio of GMCs |
| Point estimate | 0.37 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.25 |
| upper limit | 0.55 |

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

Statistical analysis description:

Ratio of GMCs (PCV/23vPS/13vPnC, PCV/PCV/13vPnC). CIs for the ratio were back transformations of a CI based on the Student t distribution for the mean difference of the logarithms of the measures (PCV/23vPS/13vPnC, PCV/PCV/13vPnC).

| Comparison groups | PCV/23vPS/13vPnC v PCV/PCV/13vPnC |
|---|---|
| Number of subjects included in analysis | 87 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | Ratio of GMCs |
| Point estimate | 0.71 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.44 |
| upper limit | 1.15 |

| **Statistical analysis title** | Common Serotype 9V |
|---|---|

Statistical analysis description:

Ratio of GMCs (PCV/23vPS/13vPnC, PCV/PCV/13vPnC). CIs for the ratio were back transformations of a CI based on the Student t distribution for the mean difference of the logarithms of the measures (PCV/23vPS/13vPnC, PCV/PCV/13vPnC).

| Comparison groups | PCV/23vPS/13vPnC v PCV/PCV/13vPnC |
|---|---|
| Number of subjects included in analysis | 87 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | Ratio of GMCs |
| Point estimate | 0.58 |

| Confidence interval | |
|---|---|
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.45 |
| upper limit | 0.75 |

| **Statistical analysis title** | Common Serotype 14 |
|---|---|

Statistical analysis description:

Ratio of GMCs (PCV/23vPS/13vPnC, PCV/PCV/13vPnC). CIs for the ratio were back transformations of a CI based on the Student t distribution for the mean difference of the logarithms of the measures (PCV/23vPS/13vPnC, PCV/PCV/13vPnC).

| Comparison groups | PCV/23vPS/13vPnC v PCV/PCV/13vPnC |
|---|---|
| Number of subjects included in analysis | 87 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | Ratio of GMCs |
| Point estimate | 0.77 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.48 |
| upper limit | 1.24 |

| **Statistical analysis title** | Common Serotype 18C |
|---|---|

Statistical analysis description:

Ratio of GMCs (PCV/23vPS/13vPnC, PCV/PCV/13vPnC). CIs for the ratio were back transformations of a CI based on the Student t distribution for the mean difference of the logarithms of the measures (PCV/23vPS/13vPnC, PCV/PCV/13vPnC).

| Comparison groups | PCV/23vPS/13vPnC v PCV/PCV/13vPnC |
|---|---|
| Number of subjects included in analysis | 87 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | Ratio of GMCs |
| Point estimate | 0.57 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.38 |
| upper limit | 0.85 |

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

Statistical analysis description:

Ratio of GMCs (PCV/23vPS/13vPnC, PCV/PCV/13vPnC). CIs for the ratio were back transformations of a CI based on the Student t distribution for the mean difference of the logarithms of the measures (PCV/23vPS/13vPnC, PCV/PCV/13vPnC).

| Comparison groups | PCV/23vPS/13vPnC v PCV/PCV/13vPnC |
|---|---|
| Number of subjects included in analysis | 87 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | Ratio of GMCs |
| Point estimate | 0.84 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.56 |
| upper limit | 1.27 |

| **Statistical analysis title** | Common Serotype 23F |
|---|---|

Statistical analysis description:

Ratio of GMCs (PCV/23vPS/13vPnC, PCV/PCV/13vPnC). CIs for the ratio were back transformations of a CI based on the Student t distribution for the mean difference of the logarithms of the measures (PCV/23vPS/13vPnC, PCV/PCV/13vPnC).

| Comparison groups | PCV/23vPS/13vPnC v PCV/PCV/13vPnC |
|---|---|
| Number of subjects included in analysis | 87 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | Ratio of GMCs |
| Point estimate | 0.64 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.44 |
| upper limit | 0.95 |

| **Statistical analysis title** | Additional Serotype 1 |
|---|---|

Statistical analysis description:

Ratio of GMCs (PCV/23vPS/13vPnC, PCV/PCV/13vPnC). CIs for the ratio were back transformations of a CI based on the Student t distribution for the mean difference of the logarithms of the measures (PCV/23vPS/13vPnC, PCV/PCV/13vPnC).

| Comparison groups | PCV/23vPS/13vPnC v PCV/PCV/13vPnC |
|---|---|
| Number of subjects included in analysis | 87 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | Ratio of GMCs |
| Point estimate | 0.27 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.18 |
| upper limit | 0.4 |

| **Statistical analysis title** | Additional Serotype 3 |
|---|---|

Statistical analysis description:

Ratio of GMCs (PCV/23vPS/13vPnC, PCV/PCV/13vPnC). CIs for the ratio were back transformations of a CI based on the Student t distribution for the mean difference of the logarithms of the measures (PCV/23vPS/13vPnC, PCV/PCV/13vPnC).

| Comparison groups | PCV/PCV/13vPnC v PCV/23vPS/13vPnC |
|---|---|
| Number of subjects included in analysis | 87 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | Ratio of GMCs |
| Point estimate | 1.14 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.76 |
| upper limit | 1.72 |

| **Statistical analysis title** | Additional Serotype 5 |
|---|---|

Statistical analysis description:

Ratio of GMCs (PCV/23vPS/13vPnC, PCV/PCV/13vPnC). CIs for the ratio were back transformations of a CI based on the Student t distribution for the mean difference of the logarithms of the measures (PCV/23vPS/13vPnC, PCV/PCV/13vPnC).

| Comparison groups | PCV/23vPS/13vPnC v PCV/PCV/13vPnC |
|---|---|
| Number of subjects included in analysis | 87 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | Ratio of GMCs |
| Point estimate | 0.36 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.25 |
| upper limit | 0.51 |

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

Statistical analysis description:

Ratio of GMCs (PCV/23vPS/13vPnC, PCV/PCV/13vPnC). CIs for the ratio were back transformations of a CI based on the Student t distribution for the mean difference of the logarithms of the measures (PCV/23vPS/13vPnC, PCV/PCV/13vPnC).

| Comparison groups | PCV/23vPS/13vPnC v PCV/PCV/13vPnC |
|---|---|

| | |
|---|---|
| Number of subjects included in analysis | 87 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | Ratio of GMCs |
| Point estimate | 0.79 |
| Confidence interval | |
|     level | 95 % |
|     sides | 2-sided |
|     lower limit | 0.55 |
|     upper limit | 1.14 |

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

Statistical analysis description:

Ratio of GMCs (PCV/23vPS/13vPnC, PCV/PCV/13vPnC). CIs for the ratio were back transformations of a CI based on the Student t distribution for the mean difference of the logarithms of the measures (PCV/23vPS/13vPnC, PCV/PCV/13vPnC).

| | |
|---|---|
| Comparison groups | PCV/PCV/13vPnC v PCV/23vPS/13vPnC |
| Number of subjects included in analysis | 87 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | Ratio of GMCs |
| Point estimate | 0.89 |
| Confidence interval | |
|     level | 95 % |
|     sides | 2-sided |
|     lower limit | 0.61 |
|     upper limit | 1.28 |

| | |
|---|---|
| **Statistical analysis title** | Additional Serotype 19A |

Statistical analysis description:

Ratio of GMCs (PCV/23vPS/13vPnC, PCV/PCV/13vPnC). CIs for the ratio were back transformations of a CI based on the Student t distribution for the mean difference of the logarithms of the measures (PCV/23vPS/13vPnC, PCV/PCV/13vPnC).

| | |
|---|---|
| Comparison groups | PCV/23vPS/13vPnC v PCV/PCV/13vPnC |
| Number of subjects included in analysis | 87 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| Parameter estimate | Ratio of GMCs |
| Point estimate | 0.86 |
| Confidence interval | |
|     level | 95 % |
|     sides | 2-sided |
|     lower limit | 0.6 |
|     upper limit | 1.23 |

## Other pre-specified: Percentage of Subjects Reporting Prespecified Local Reactions Within 4 Days of Vaccination

| End point title | Percentage of Subjects Reporting Prespecified Local Reactions Within 4 Days of Vaccination |
|---|---|

End point description:

Local reactions were reported by the parent/legal guardian using a diary card. Tenderness was scaled as Any (tenderness present); Significant (present and interfered with limb movement). Redness and swelling were scaled as Any (redness or swelling present); Mild (0.5 centimeters [cm] to 2.0 cm); Moderate (2.5 to 7.0 cm); Severe (greater than [>] 7.0 cm). Subjects may have been represented in more than 1 category. Safety population, included all subjects who received at least 1 dose of the study vaccine; n=number of subjects reporting the specific characteristic.

| End point type | Other pre-specified |
|---|---|

End point timeframe:

Day 1 through Day 4

| End point values | PCV/23vPS/13 vPnC | PCV/PCV/13vP nC | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 50[11] | 39[12] | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | | | | |
| Tenderness: Any (n=44, 30) | 88 | 76.9 | | |
| Tenderness: Significant (n=6, 8) | 12 | 20.5 | | |
| Redness: Any (n=25, 26) | 50 | 66.7 | | |
| Redness: Mild (n=5, 6) | 10 | 15.8 | | |
| Redness: Moderate (n=20, 20) | 40 | 52.6 | | |
| Redness: Severe (n=5, 8) | 10 | 21.1 | | |
| Swelling: Any (n=22, 23) | 44 | 59 | | |
| Swelling: Mild (n=8, 10) | 16.3 | 26.3 | | |
| Swelling: Moderate (n=14, 17) | 28.6 | 44.7 | | |
| Swelling: Severe (n=1, 3) | 2 | 7.9 | | |

Notes:

[11] - N=number of subjects reporting yes for at least 1 day or no for all days.

[12] - N=number of subjects reporting yes for at least 1 day or no for all days.

## Statistical analyses

| Statistical analysis title | Comparing Any Tenderness |
|---|---|
| Comparison groups | PCV/23vPS/13vPnC v PCV/PCV/13vPnC |
| Number of subjects included in analysis | 89 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | = 0.253 |
| Method | Fisher exact |

| Statistical analysis title | Comparing Significant Tenderness |
|---|---|
| Comparison groups | PCV/23vPS/13vPnC v PCV/PCV/13vPnC |

| Number of subjects included in analysis | 89 |
|---|---|
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | = 0.38 |
| Method | Fisher exact |

| **Statistical analysis title** | Comparing Any Redness |
|---|---|
| Comparison groups | PCV/23vPS/13vPnC v PCV/PCV/13vPnC |
| Number of subjects included in analysis | 89 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | = 0.135 |
| Method | Fisher exact |

| **Statistical analysis title** | Comparing Mild Redness |
|---|---|
| Comparison groups | PCV/23vPS/13vPnC v PCV/PCV/13vPnC |
| Number of subjects included in analysis | 89 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | = 0.52 |
| Method | Fisher exact |

| **Statistical analysis title** | Comparing Moderate Redness |
|---|---|
| Comparison groups | PCV/23vPS/13vPnC v PCV/PCV/13vPnC |
| Number of subjects included in analysis | 89 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | = 0.283 |
| Method | Fisher exact |

| **Statistical analysis title** | Comparing Severe Redness |
|---|---|
| Comparison groups | PCV/23vPS/13vPnC v PCV/PCV/13vPnC |
| Number of subjects included in analysis | 89 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | = 0.225 |
| Method | Fisher exact |

| Statistical analysis title | Comparing Any Swelling |
|---|---|
| Comparison groups | PCV/23vPS/13vPnC v PCV/PCV/13vPnC |
| Number of subjects included in analysis | 89 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | = 0.202 |
| Method | Fisher exact |

| Statistical analysis title | Comparing Mild Swelling |
|---|---|
| Comparison groups | PCV/23vPS/13vPnC v PCV/PCV/13vPnC |
| Number of subjects included in analysis | 89 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | = 0.294 |
| Method | Fisher exact |

| Statistical analysis title | Comparing Moderate Swelling |
|---|---|
| Comparison groups | PCV/23vPS/13vPnC v PCV/PCV/13vPnC |
| Number of subjects included in analysis | 89 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | = 0.175 |
| Method | Fisher exact |

| Statistical analysis title | Comparing Severe Swelling |
|---|---|
| Comparison groups | PCV/23vPS/13vPnC v PCV/PCV/13vPnC |
| Number of subjects included in analysis | 89 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | = 0.314 |
| Method | Fisher exact |

**Other pre-specified: Percentage of Subjects Reporting Prespecified Systemic Reactions Within 4 Days of Vaccination**

| End point title | Percentage of Subjects Reporting Prespecified Systemic Reactions Within 4 Days of Vaccination |
|---|---|
| End point description: | |

Pre-specified systemic events (any fever 38 degrees Celsius [C], decreased appetite, irritability, increased sleep, and decreased sleep) were reported using a diary card. Subjects may have been represented in more than 1 category. Safety population; n=number of subjects reporting the specific characteristic

| End point type | Other pre-specified |
|---|---|

| End point values | PCV/23vPS/13 vPnC | PCV/PCV/13vP nC | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 50[13] | 39[14] | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | | | | |
| Fever ≥ 38 degrees C but ≤ 39 degrees C (n=1, 1) | 2 | 2.8 | | |
| Decreased appetite (n=6, 4) | 12.2 | 10.3 | | |
| Irritability (n=9, 4) | 18.4 | 11.4 | | |
| Increased sleep (n=2, 5) | 4 | 12.8 | | |
| Decreased sleep (n=0, 2) | 0 | 5.1 | | |
| Rash (n=3, 1) | 6 | 2.6 | | |

Notes:

[13] - N=number of subjects reporting yes for at least 1 day or no for all days.

[14] - N=number of subjects reporting yes for at least 1 day or no for all days.

## Statistical analyses

| Statistical analysis title | Comparing: Fever ≥ 38 Degrees C But ≤ 39 Degrees C |
|---|---|
| Comparison groups | PCV/23vPS/13vPnC v PCV/PCV/13vPnC |
| Number of subjects included in analysis | 89 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | > 0.99 |
| Method | Fisher exact |

| Statistical analysis title | Comparing Decreased Appetite |
|---|---|
| Comparison groups | PCV/23vPS/13vPnC v PCV/PCV/13vPnC |
| Number of subjects included in analysis | 89 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | > 0.99 |
| Method | Fisher exact |

| Statistical analysis title | Comparing Irritability |
|---|---|
| Comparison groups | PCV/23vPS/13vPnC v PCV/PCV/13vPnC |

| Number of subjects included in analysis | 89 |
|---|---|
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | = 0.543 |
| Method | Fisher exact |

| **Statistical analysis title** | Comparing Increased Sleep |
|---|---|
| Comparison groups | PCV/23vPS/13vPnC v PCV/PCV/13vPnC |
| Number of subjects included in analysis | 89 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | = 0.233 |
| Method | Fisher exact |

| **Statistical analysis title** | Comparing Decreased Sleep |
|---|---|
| Comparison groups | PCV/23vPS/13vPnC v PCV/PCV/13vPnC |
| Number of subjects included in analysis | 89 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | = 0.198 |
| Method | Fisher exact |

| **Statistical analysis title** | Comparing Rash |
|---|---|
| Comparison groups | PCV/PCV/13vPnC v PCV/23vPS/13vPnC |
| Number of subjects included in analysis | 89 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | = 0.628 |
| Method | Fisher exact |

# Adverse events

## Adverse events information

| | |
|---|---|
| Timeframe for reporting adverse events: | |
| Baseline through 1 Month after last study vaccination (28 Days). Local reactions and systemic events assessed within 4 days of dose (Day 1 through Day 4) | |
| Adverse event reporting additional description: | |
| Same event may appear as both an adverse event (AE) and a serious adverse event (SAE). However, what is presented are distinct events. An event may be categorized as serious in one subject, as non-serious in another subject, or one subject may have experienced both the events. Version was not captured, here 0.0 is mentioned for dictionary version. | |
| Assessment type | Non-systematic |

## Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 0.0 |

## Reporting groups

| | |
|---|---|
| Reporting group title | PCV/23vPS/13vPnC |

Reporting group description:

For this study, subjects received a single dose of 13vPnC. Subjects previously must have also received an infant series of 9V-MnCC also known as PCV followed by a toddler dose of 23vPS. Other AEs (non-serious events): the number affected (N) for nonsystematic (unsolicited) Other AEs N=8; systematic (solicited) Local Reactions N=44; systematic (solicited) Systemic Events N=9. Subjects affected and occurrences for Local Reactions (LRs) and Systemic Events (SEs) is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.

| | |
|---|---|
| Reporting group title | PCV/PCV/13vPnC |

Reporting group description:

For this study, subjects received a single dose of 13vPnC. Subjects must have also previously received 9V-MnCC followed by a toddler dose of 9V-MnCC (also referred to as PCV). Other AEs (non-serious events): the number affected (N) for nonsystematic (unsolicited) Other Adverse Events N=7; systematic (solicited) Local Reactions N=30; systematic (solicited) Systemic Events N=5. Subjects affected and occurrences for LRs and SEs is same as data collected through e-diaries cannot be used to distinguish one occurrence from another within a subject/vaccination.

| Serious adverse events | PCV/23vPS/13vPnC | PCV/PCV/13vPnC | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
|     subjects affected / exposed | 0 / 50 (0.00%) | 0 / 39 (0.00%) | |
|     number of deaths (all causes) | 0 | 0 | |
|     number of deaths resulting from adverse events | 0 | 0 | |

Frequency threshold for reporting non-serious adverse events: 0 %

| Non-serious adverse events | PCV/23vPS/13vPnC | PCV/PCV/13vPnC | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
|     subjects affected / exposed | 44 / 50 (88.00%) | 30 / 39 (76.92%) | |
| Injury, poisoning and procedural complications | | | |

| | | | |
|---|---|---|---|
| Fall | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | 1 / 39 (2.56%) | |
| occurrences (all) | 0 | 1 | |
| **Blood and lymphatic system disorders** | | | |
| Lymphadenopathy | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | 0 / 39 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| **General disorders and administration site conditions** | | | |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | 0 / 39 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Fever ≥ 38°C but ≤ 39°C | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed[1] | 1 / 49 (2.04%) | 1 / 36 (2.78%) | |
| occurrences (all) | 1 | 1 | |
| Decreased appetite | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed[2] | 6 / 49 (12.24%) | 4 / 39 (10.26%) | |
| occurrences (all) | 6 | 4 | |
| Irritability | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed[3] | 9 / 49 (18.37%) | 4 / 35 (11.43%) | |
| occurrences (all) | 9 | 4 | |
| Increased sleep | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 2 / 50 (4.00%) | 5 / 39 (12.82%) | |
| occurrences (all) | 2 | 5 | |
| Decreased sleep | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed[4] | 0 / 48 (0.00%) | 2 / 39 (5.13%) | |
| occurrences (all) | 0 | 2 | |
| Rash | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 3 / 50 (6.00%) | 1 / 39 (2.56%) | |
| occurrences (all) | 3 | 1 | |

| | | |
|---|---|---|
| **Tenderness (Any)** | | |
| alternative assessment type: Systematic | | |
| subjects affected / exposed | 44 / 50 (88.00%) | 30 / 39 (76.92%) |
| occurrences (all) | 44 | 30 |
| **Tenderness (Significant)** | | |
| alternative assessment type: Systematic | | |
| subjects affected / exposed | 6 / 50 (12.00%) | 8 / 39 (20.51%) |
| occurrences (all) | 6 | 8 |
| **Redness (Any)** | | |
| alternative assessment type: Systematic | | |
| subjects affected / exposed | 25 / 50 (50.00%) | 26 / 39 (66.67%) |
| occurrences (all) | 25 | 26 |
| **Redness (Mild)** | | |
| alternative assessment type: Systematic | | |
| subjects affected / exposed[5] | 5 / 50 (10.00%) | 6 / 38 (15.79%) |
| occurrences (all) | 5 | 6 |
| **Redness (Moderate)** | | |
| alternative assessment type: Systematic | | |
| subjects affected / exposed[6] | 20 / 50 (40.00%) | 20 / 38 (52.63%) |
| occurrences (all) | 20 | 20 |
| **Redness (Severe)** | | |
| alternative assessment type: Systematic | | |
| subjects affected / exposed[7] | 5 / 50 (10.00%) | 8 / 38 (21.05%) |
| occurrences (all) | 5 | 8 |
| **Swelling (Any)** | | |
| alternative assessment type: Systematic | | |
| subjects affected / exposed | 22 / 50 (44.00%) | 23 / 39 (58.97%) |
| occurrences (all) | 22 | 23 |
| **Swelling (Mild)** | | |
| alternative assessment type: Systematic | | |
| subjects affected / exposed[8] | 8 / 49 (16.33%) | 10 / 38 (26.32%) |
| occurrences (all) | 8 | 10 |
| **Swelling (Moderate)** | | |
| alternative assessment type: Systematic | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed[9] | 14 / 49 (28.57%) | 17 / 38 (44.74%) | |
| occurrences (all) | 14 | 17 | |
| Swelling (Severe) | | | |
| subjects affected / exposed[10] | 1 / 49 (2.04%) | 3 / 38 (7.89%) | |
| occurrences (all) | 1 | 3 | |
| **Gastrointestinal disorders** | | | |
| Vomiting | | | |
| subjects affected / exposed | 2 / 50 (4.00%) | 1 / 39 (2.56%) | |
| occurrences (all) | 2 | 1 | |
| Diarrhoea | | | |
| subjects affected / exposed | 2 / 50 (4.00%) | 0 / 39 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | 0 / 39 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | 1 / 39 (2.56%) | |
| occurrences (all) | 0 | 1 | |
| **Respiratory, thoracic and mediastinal disorders** | | | |
| Epistaxis | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | 0 / 39 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| **Skin and subcutaneous tissue disorders** | | | |
| Urticaria | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | 0 / 39 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| **Infections and infestations** | | | |
| Viral infection | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | 3 / 39 (7.69%) | |
| occurrences (all) | 0 | 5 | |
| Influenza | | | |
| subjects affected / exposed | 1 / 50 (2.00%) | 1 / 39 (2.56%) | |
| occurrences (all) | 1 | 1 | |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 50 (0.00%) | 1 / 39 (2.56%) | |
| occurrences (all) | 0 | 1 | |

| Pharyngitis | | |
|---|---|---|
| subjects affected / exposed | 1 / 50 (2.00%) | 0 / 39 (0.00%) |
| occurrences (all) | 1 | 0 |

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Here number of subjects exposed signifies subjects reporting yes for at least 1 day or no for all days.
[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Here number of subjects exposed signifies subjects reporting yes for at least 1 day or no for all days.
[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Here number of subjects exposed signifies subjects reporting yes for at least 1 day or no for all days.
[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Here number of subjects exposed signifies subjects reporting yes for at least 1 day or no for all days.
[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Here number of subjects exposed signifies subjects reporting yes for at least 1 day or no for all days.
[6] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Here number of subjects exposed signifies subjects reporting yes for at least 1 day or no for all days.
[7] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Here number of subjects exposed signifies subjects reporting yes for at least 1 day or no for all days.
[8] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Here number of subjects exposed signifies subjects reporting yes for at least 1 day or no for all days.
[9] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Here number of subjects exposed signifies subjects reporting yes for at least 1 day or no for all days.
[10] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Here number of subjects exposed signifies subjects reporting yes for at least 1 day or no for all days.

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol?  Yes

| Date | Amendment |
|---|---|
| 13 April 2009 | Minor clarification was made to temporary delay criterion, as recommended by the Icelandic Medicines Control Agency, to clarify timing of antibiotic therapy and treatment with oral steroid agents. |

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial?  No

## Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

In protocol, primary analysis was based on all available immunogenicity population and later modified to evaluable immunogenicity population in Statistical Analysis Plan based on subsequent similar studies and suitability for primary objective.

Notes: