# Clinical trial results:
# A phase III long-term follow-up study to assess the immune responses following vaccination at 36-46 months of age with a booster dose of GSK Biologicals' 10-valent pneumococcal conjugate vaccine (10Pn-PD-DiT) and to evaluate the immunogenicity and safety of a 2-dose catch-up immunization course with the 10Pn-PD-DiT vaccine in the fourth year of life.

## Summary

| | |
|---|---|
| EudraCT number | 2008-003950-14 |
| Trial protocol | SK SE |
| Global end of trial date | 02 July 2009 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 05 April 2016 |
| First version publication date | 04 April 2015 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | 111736 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00984139 |
| WHO universal trial number (UTN) | - |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | GlaxoSmithKline Biologicals |
| Sponsor organisation address | Rue de l'Institut 89, Rixensart, Belgium, B-1330 |
| Public contact | Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089-904466, GSKClinicalSupportHD@gsk.com |
| Scientific contact | Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089-904466, GSKClinicalSupportHD@gsk.com |

Notes:

**Paediatric regulatory details**

| | |
|---|---|
| Is trial part of an agreed paediatric investigation plan (PIP) | Yes |
| EMA paediatric investigation plan number(s) | EMEA-000673-PIP01-09 |
| 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? | No |

Notes:

## Results analysis stage

| | |
|---|---|
| Analysis stage | Final |
| Date of interim/final analysis | 12 November 2009 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 02 July 2009 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

To assess the immune responses following vaccination with a booster dose of the 10Pn-PD-DiT vaccine administered at 36-46 months of age in children previously vaccinated with the 10Pn-PD-DiT vaccine in study 10PN-PD-DIT-002 (105539) according to either a 3-dose or 2-dose primary vaccination within the first 6 months of age and booster vaccination at 11 months of age and to assess the immune responses following vaccination with a single dose of the 10Pn-PD-DiT vaccine in age-matched unprimed children.

Protection of trial subjects:

All subjects were supervised after vaccination/product administration with appropriate medical treatment readily available. Vaccines/products were administered by qualified and trained personnel. Vaccines/products were administered only to eligible subjects that had no contraindications to any components of the vaccines/products. Subjects were followed-up for minimum 30 days after the last vaccination/product administration.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 02 December 2008 |
| 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 | Slovakia: 85 |
| Country: Number of subjects enrolled | Sweden: 87 |
| Worldwide total number of subjects | 172 |
| EEA total number of subjects | 172 |

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 | 0 |

| | |
|---|---|
| months) | |
| Children (2-11 years) | 172 |
| 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: -

### Pre-assignment period milestones

| | |
|---|---|
| Number of subjects started | 172 |
| Number of subjects completed | 172 |

### Period 1

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

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | 10Pn-2d group |

Arm description:

Subjects previously vaccinated with the 10Pn-PD-DiT vaccine according to a 2+1 schedule, receiving one dose of 10Pn-PD-DiT at 36-46 months of age, i.e. 24-34 months after the last dose given in study 10PN-PD-DIT-002 (105539).

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Synflorix™ |
| Investigational medicinal product code | |
| Other name | 10Pn-PD-DiT |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Subjects received one additional dose of 10Pn-PD-DiT at 36-46 months of age, i.e. 24-34 months after the last dose given in study 10PN-PD-DIT-002 (105539) administered intramuscularly in the right deltoid

| | |
|---|---|
| **Arm title** | 10Pn-3d group |

Arm description:

Subjects previously vaccinated with the 10Pn-PD-DiT vaccine according to a 3+1 schedule, receiving one dose of 10Pn-PD-DiT at 36-46 months of age, i.e. 24-34 months after the last dose given in study 10PN-PD-DIT-002 (105539).

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Synflorix™ |
| Investigational medicinal product code | |
| Other name | 10Pn-PD-DiT |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Subjects received one additional dose of 10Pn-PD-DiT at 36-46 months of age, i.e. 24-34 months after the last dose given in study 10PN-PD-DIT-002 (105539) administered intramuscularly in the right deltoid

| | |
|---|---|
| **Arm title** | Unprimed group |

Arm description:

Age-matched subjects not previously vaccinated with any pneumococcal vaccine receiving two doses of 10Pn-PD-DiT at 36-46 and 38-48 months of age. Age-matching was ensured by the enrolment of subjects 36-46 months of age.

| | |
|---|---|
| Arm type | Active comparator |
| Investigational medicinal product name | Synflorix™ |
| Investigational medicinal product code | |
| Other name | 10Pn-PD-DiT |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Subject received 2 doses of 10Pn-PD-DiT at 36-46 and 38-48 months of age, administered intramuscularly in the right deltoid.

| **Number of subjects in period 1** | 10Pn-2d group | 10Pn-3d group | Unprimed group |
|---|---|---|---|
| Started | 51 | 59 | 62 |
| Completed | 51 | 58 | 62 |
| Not completed | 0 | 1 | 0 |
| Consent withdrawn by subject | - | 1 | - |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | 10Pn-2d group |
| Reporting group description: | |
| Subjects previously vaccinated with the 10Pn-PD-DiT vaccine according to a 2+1 schedule, receiving one dose of 10Pn-PD-DiT at 36-46 months of age, i.e. 24-34 months after the last dose given in study 10PN-PD-DIT-002 (105539). | |
| Reporting group title | 10Pn-3d group |
| Reporting group description: | |
| Subjects previously vaccinated with the 10Pn-PD-DiT vaccine according to a 3+1 schedule, receiving one dose of 10Pn-PD-DiT at 36-46 months of age, i.e. 24-34 months after the last dose given in study 10PN-PD-DIT-002 (105539). | |
| Reporting group title | Unprimed group |
| Reporting group description: | |
| Age-matched subjects not previously vaccinated with any pneumococcal vaccine receiving two doses of 10Pn-PD-DiT at 36-46 and 38-48 months of age. Age-matching was ensured by the enrolment of subjects 36-46 months of age. | |

| Reporting group values | 10Pn-2d group | 10Pn-3d group | Unprimed group |
|---|---|---|---|
| Number of subjects | 51 | 59 | 62 |
| Age categorical<br>Units: Subjects | | | |
| In utero | | | |
| Preterm newborn infants (gestational age < 37 wks) | | | |
| Newborns (0-27 days) | | | |
| Infants and toddlers (28 days-23 months) | | | |
| Children (2-11 years) | | | |
| Adolescents (12-17 years) | | | |
| Adults (18-64 years) | | | |
| From 65-84 years | | | |
| 85 years and over | | | |
| Age continuous<br>Units: months | | | |
| arithmetic mean | 38.2 | 38 | 40.1 |
| standard deviation | ± 1.83 | ± 1.81 | ± 2.64 |
| Gender categorical<br>Units: Subjects | | | |
| Female | 25 | 25 | 31 |
| Male | 26 | 34 | 31 |

| Reporting group values | Total | | |
|---|---|---|---|
| Number of subjects | 172 | | |
| Age categorical<br>Units: Subjects | | | |
| In utero | 0 | | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | | |
| Newborns (0-27 days) | 0 | | |

| | | | |
|---|---|---|---|
| Infants and toddlers (28 days-23 months) | 0 | | |
| Children (2-11 years) | 0 | | |
| Adolescents (12-17 years) | 0 | | |
| Adults (18-64 years) | 0 | | |
| From 65-84 years | 0 | | |
| 85 years and over | 0 | | |
| Age continuous | | | |
| Units: months | | | |
| arithmetic mean | | | |
| standard deviation | - | | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 81 | | |
| Male | 91 | | |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | 10Pn-2d group |

Reporting group description:

Subjects previously vaccinated with the 10Pn-PD-DiT vaccine according to a 2+1 schedule, receiving one dose of 10Pn-PD-DiT at 36-46 months of age, i.e. 24-34 months after the last dose given in study 10PN-PD-DIT-002 (105539).

| | |
|---|---|
| Reporting group title | 10Pn-3d group |

Reporting group description:

Subjects previously vaccinated with the 10Pn-PD-DiT vaccine according to a 3+1 schedule, receiving one dose of 10Pn-PD-DiT at 36-46 months of age, i.e. 24-34 months after the last dose given in study 10PN-PD-DIT-002 (105539).

| | |
|---|---|
| Reporting group title | Unprimed group |

Reporting group description:

Age-matched subjects not previously vaccinated with any pneumococcal vaccine receiving two doses of 10Pn-PD-DiT at 36-46 and 38-48 months of age. Age-matching was ensured by the enrolment of subjects 36-46 months of age.

### Primary: Antibody Geometric Mean Concentrations (GMCs) against the vaccine pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F in the Unprimed group

| | |
|---|---|
| End point title | Antibody Geometric Mean Concentrations (GMCs) against the vaccine pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F in the Unprimed group[1][2] |

End point description:

Antibodies assessed for this outcome measure were those against the vaccine pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C,19F and 23F (ANTI-1, -4, -5, -6B, -7F, -9V, -14, -18C, -19F and -23F). Antibody concentrations were measured by 22F enzyme-linked immunosorbent assay (ELISA), expressed as geometric mean concentrations (GMCs), in micrograms per milliliter (µg/mL). The seropositivity cut-off of the assay was an antibody concentration ≥ 0.05 µg/mL. The results presented for the time point 7-10 days after dose 1 (Day 7), correspond to the primary outcome.

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

End point timeframe:

Pre-vaccination (PRE), one week after dose 1 (Day 7) and one month after dose 2 (Month 3)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.
[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: When time frames are not the same for the 3 groups for a same endpoint, the endpoint has been duplicated: the first one for presenting results in the 10Pn-2d and 10Pn-3d groups and the second one for presenting the results in the Unprimed group.

| End point values | Unprimed group | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 60 | | | |
| Units: µg/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-1 at PRE (N= 60) | 0.06 (0.05 to 0.08) | | | |

| | | | | |
|---|---|---|---|---|
| Anti-1 at Day 7 (N= 60) | 0.6 (0.47 to 0.76) | | | |
| Anti-1 at Month 3 (N= 60) | 2.81 (2.25 to 3.51) | | | |
| Anti-4 at PRE (N= 60) | 0.04 (0.03 to 0.05) | | | |
| Anti-4 at Day 7 (N= 60) | 2.37 (1.91 to 2.94) | | | |
| Anti-4 at Month 3 (N= 60) | 8.44 (7.16 to 9.94) | | | |
| Anti-5 at PRE (N= 60) | 0.07 (0.05 to 0.09) | | | |
| Anti-5 at Day 7 (N= 60) | 0.45 (0.34 to 0.59) | | | |
| Anti-5 at Month 3 (N= 60) | 3.54 (2.96 to 4.23) | | | |
| Anti-6B at PRE (N= 60) | 0.1 (0.07 to 0.13) | | | |
| Anti-6B at Day 7 (N= 58) | 0.2 (0.14 to 0.29) | | | |
| Anti-6B at Month 3 (N= 60) | 1.11 (0.84 to 1.46) | | | |
| Anti-7F at PRE (N= 60) | 0.08 (0.05 to 0.12) | | | |
| Anti-7F at Day 7 (N= 60) | 0.92 (0.67 to 1.25) | | | |
| Anti-7F at Month 3 (N= 60) | 6.1 (4.99 to 7.46) | | | |
| Anti-9V at PRE (N= 60) | 0.05 (0.04 to 0.07) | | | |
| Anti-9V at Day 7 (N= 60) | 0.33 (0.23 to 0.48) | | | |
| Anti-9V at Month 3 (N= 60) | 2.22 (1.74 to 2.82) | | | |
| Anti-14 at PRE (N= 60) | 0.25 (0.16 to 0.38) | | | |
| Anti-14 at Day 7 (N= 60) | 0.54 (0.34 to 0.86) | | | |
| Anti-14 at Month 3 (N= 60) | 6.48 (4.98 to 8.44) | | | |
| Anti-18C at PRE (N= 60) | 0.06 (0.04 to 0.08) | | | |
| Anti-18C at Day 7 (N= 59) | 1.45 (1.01 to 2.06) | | | |
| Anti-18C at Month 3 (N= 60) | 22.28 (18.14 to 27.36) | | | |
| Anti-19F at PRE (N= 60) | 0.23 (0.14 to 0.38) | | | |
| Anti-19F at Day 7 (N= 59) | 1.82 (1.27 to 2.6) | | | |
| Anti-19F at Month 3 (N= 60) | 17.03 (13.38 to 21.68) | | | |
| Anti-23F at PRE (N= 60) | 0.06 (0.04 to 0.08) | | | |
| Anti-23F at Day 7 (N= 60) | 0.1 (0.07 to 0.15) | | | |
| Anti-23F at Month 3 (N= 60) | 1.09 (0.81 to 1.45) | | | |

## Statistical analyses

No statistical analyses for this end point

## Primary: Antibody Geometric Mean Concentrations (GMCs) against the vaccine pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F in the 10Pn-2d and 10Pn-3d groups

| End point title | Antibody Geometric Mean Concentrations (GMCs) against the vaccine pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F in the 10Pn-2d and 10Pn-3d groups[3][4] |
|---|---|

End point description:

Antibodies assessed for this outcome measure were those against the vaccine pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C,19F and 23F (ANTI-1, -4, -5, -6B, -7F, -9V, -14, -18C, -19F and -23F). Antibody concentrations were measured by 22F enzyme-linked immunosorbent assay (ELISA), expressed as geometric mean concentrations (GMCs), in micrograms per milliliter (µg/mL). The seropositivity cut-off of the assay was an antibody concentration ≥ 0.05 µg/mL. The results presented for the time point 7-10 days after immunization (Mth34+D7), correspond to the primary outcome.

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

End point timeframe:

1 month after booster dose (Month 10) –in primary study 105539), pre-additional dose at Month 34 in the current study (Month 34) and one week after vaccination at Mont 34+7 days (Mth34+D7)

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.
[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: When time frames are not the same for the 3 groups for a same endpoint, the endpoint has been duplicated: the first one for presenting results in the 10Pn-2d and 10Pn-3d groups and the second one for presenting the results in the Unprimed group.

| **End point values** | 10Pn-2d group | 10Pn-3d group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 50 | 57 | | |
| Units: µg/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-1 at Month 10 (N=50,57) | 1.91 (1.52 to 2.42) | 1.87 (1.49 to 2.33) | | |
| Anti-1 at Month 34 (N=49,57) | 0.13 (0.1 to 0.17) | 0.17 (0.14 to 0.22) | | |
| Anti-1 at Mth34+D7(N=50,55) | 4.06 (3.2 to 5.15) | 4.72 (3.77 to 5.92) | | |
| Anti-4 at Month 10 (N=50,57) | 2.97 (2.34 to 3.77) | 3.2 (2.62 to 3.91) | | |
| Anti-4 at Month 34 (N=48,54) | 0.15 (0.1 to 0.23) | 0.19 (0.14 to 0.25) | | |
| Anti-4 at Mth34+D (N=49,55) | 7.54 (5.98 to 9.5) | 9.97 (7.68 to 12.95) | | |
| Anti-5 at Month 10 (N=50,57) | 2.71 (2.15 to 3.41) | 3.01 (2.4 to 3.76) | | |
| Anti-5 at Month 34 (N=50,57) | 0.24 (0.19 to 0.31) | 0.33 (0.26 to 0.42) | | |
| Anti-5 at Mth34+D (N=50,55) | 5.38 (4.09 to 7.08) | 7.07 (5.51 to 9.09) | | |
| Anti-6B at Month 10 (N=50,57) | 0.9 (0.59 to 1.36) | 1.62 (1.16 to 2.27) | | |
| Anti-6B at Month 34 (N=48,57) | 0.5 (0.29 to 0.88) | 1.01 (0.62 to 1.64) | | |

| | | | | |
|---|---|---|---|---|
| Anti-6B at Mth34+D7 (N=50,55) | 4 (2.82 to 5.69) | 6.33 (4.75 to 8.45) | | |
| Anti-7F at Month 10 (N=50,57) | 2.94 (2.4 to 3.59) | 3.88 (3.23 to 4.65) | | |
| Anti-7F at Month 34 (N=49,56) | 0.33 (0.24 to 0.46) | 0.51 (0.42 to 0.61) | | |
| Anti-7F at Mth34+D7 (N=50,55) | 6.18 (5.05 to 7.56) | 7.27 (5.87 to 9.01) | | |
| Anti-9V at Month 10 (N=50,57) | 2.59 (2.03 to 3.31) | 3.81 (3.11 to 4.67) | | |
| Anti-9V at Month 34 (N=50,57) | 0.24 (0.18 to 0.33) | 0.49 (0.34 to 0.69) | | |
| Anti-9V at Mth34+D7 (N=50,55) | 7.48 (5.88 to 9.51) | 10.17 (7.86 to 13.16) | | |
| Anti-14 at Month 10 (N=50,57) | 3.91 (3.05 to 5) | 5.22 (4.22 to 6.46) | | |
| Anti-14 at Month 34 (N=50,56) | 0.62 (0.39 to 0.97) | 1.1 (0.69 to 1.75) | | |
| Anti-14 at Mth34+D7 (N=50,55) | 13.42 (9.7 to 18.55) | 19.67 (14.97 to 25.84) | | |
| Anti-18C at Month 10 (N=50,57) | 4.87 (3.77 to 6.29) | 5.52 (4.2 to 7.26) | | |
| Anti-18C at Month 34 (N=50,56) | 0.37 (0.26 to 0.54) | 0.49 (0.35 to 0.7) | | |
| Anti-18C at Mth34+D7 (N=50,55) | 17.12 (12.77 to 22.94) | 22.62 (17.58 to 29.11) | | |
| Anti-19F at Month 10 (N=50,57) | 6.68 (5.2 to 8.59) | 6.6 (5.16 to 8.46) | | |
| Anti-19F at Month 34 (N=47,56) | 1.42 (0.8 to 2.51) | 1.44 (0.82 to 2.53) | | |
| Anti-19F at Mth34+D7 (N=50,55) | 20.28 (15.71 to 26.19) | 30.55 (24.32 to 38.37) | | |
| Anti-23F at Month 10 (N=50,57) | 2.12 (1.52 to 2.97) | 2.67 (1.99 to 3.59) | | |
| Anti-23F at Month 34 (N=49,56) | 0.41 (0.23 to 0.71) | 0.67 (0.41 to 1.11) | | |
| Anti-23F at Mth34+D7 (N=50,55) | 6.23 (4.34 to 8.94) | 8.42 (6.38 to 11.11) | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with Anti-pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F antibody concentrations ≥ 0.05 µg/mL in the 10Pn-2d and 10Pn-3d groups

| | |
|---|---|
| End point title | Number of subjects with Anti-pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F antibody concentrations ≥ 0.05 µg/mL in the 10Pn-2d and 10Pn-3d groups[5] |

End point description:

Antibodies assessed for this outcome measure were those against the vaccine pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C,19F and 23F (ANTI-1, -4, -5, -6B, -7F, -9V, -14, -18C, -19F and -23F). Antibody concentrations were measured by 22F enzyme-linked immunosorbent assay (ELISA), expressed as geometric mean concentrations (GMCs), in micrograms per milliliter (µg/mL). The seropositivity cut-off of the assay was an antibody concentration ≥ 0.05 µg/mL..

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

End point timeframe:

1 month after booster dose (Month 10) –in primary study 105539), pre-additional dose at Month 34 in

the current study (Month 34) and one week after vaccination at Mont 34+7 days (Mth34+D7)

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: When time frames are not the same for the 3 groups for a same endpoint, the endpoint has been duplicated: the first one for presenting results in the 10Pn-2d and 10Pn-3d groups and the second one for presenting the results in the Unprimed group.

| **End point values** | 10Pn-2d group | 10Pn-3d group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 50 | 57 | | |
| Units: Subjects | | | | |
| Anti-1 at Month 10 (N=50,57) | 50 | 57 | | |
| Anti-1 at Month 34 (N=49,57) | 43 | 55 | | |
| Anti-1 at Mth34+D7(N=50,55) | 50 | 55 | | |
| Anti-4 at Month 10 (N=50,57) | 50 | 57 | | |
| Anti-4 at Month 34 (N=48,54) | 41 | 54 | | |
| Anti-4 at Mth34+D7(N=49,55) | 49 | 55 | | |
| Anti-5 at Month 10 (N=50,57) | 50 | 57 | | |
| Anti-5 at Month 34 (N=50,57) | 49 | 57 | | |
| Anti-5 at Mth34+D7(N=50,55) | 50 | 55 | | |
| Anti-6B at Month 10 (N=50,57) | 45 | 54 | | |
| Anti-6B at Month 34 (N=48,57) | 43 | 56 | | |
| Anti-6B at Mth34+D7(N=50,55) | 50 | 55 | | |
| Anti-7F at Month 10 (N=50,57) | 50 | 57 | | |
| Anti-7F at Month 34 (N=49,56) | 47 | 56 | | |
| Anti-7F at Mth34+D7(N=50,55) | 50 | 55 | | |
| Anti-9V at Month 10 (N=50,57) | 50 | 57 | | |
| Anti-9V at Month 34 (N=50,57) | 48 | 56 | | |
| Anti-9V at Mth34+D7(N=50,55) | 50 | 55 | | |
| Anti-14 at Month 10 (N=50,57) | 50 | 57 | | |
| Anti-14 at Month 34 (N=50,56) | 50 | 56 | | |
| Anti-14 at Mth34+D7 (N=50,55 | 50 | 55 | | |
| Anti-18C at Month 10 (N=50,57 | 50 | 57 | | |
| Anti-18C at Month 34 (N=50,56) | 48 | 56 | | |
| Anti-18C at Mth34+D7(N=50,55) | 50 | 55 | | |
| Anti-19F at Month 10 (N=50,57) | 50 | 57 | | |
| Anti-19F at Month 34 (N=47,56) | 47 | 56 | | |
| Anti-19F at Mth34+D7(N=50,55) | 50 | 55 | | |
| Anti-23F at Month 10 (N=50,57) | 49 | 56 | | |
| Anti-23F at Month 34 (N=49,56) | 43 | 56 | | |
| Anti-23F at Mth34+D7(N=50,55) | 49 | 55 | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with Anti-pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F antibody concentrations ≥ 0.05 µg/mL in the Unprimed group

| End point title | Number of subjects with Anti-pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F antibody concentrations ≥ 0.05 µg/mL in the Unprimed group[6] |
|---|---|

End point description:

Antibodies assessed for this outcome measure were those against the vaccine pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C,19F and 23F (ANTI-1, -4, -5, -6B, -7F, -9V, -14, -18C, -19F and -23F). Antibody concentrations were measured by 22F enzyme-linked immunosorbent assay (ELISA), expressed as geometric mean concentrations (GMCs), in micrograms per milliliter (µg/mL). The seropositivity cut-off of the assay was an antibody concentration ≥ 0.05 µg/mL.

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

End point timeframe:

Pre-vaccination (PRE), one week after dose 1 (Day 7) and one month after dose 2 (Month 3)

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: When time frames are not the same for the 3 groups for a same endpoint, the endpoint has been duplicated: the first one for presenting results in the 10Pn-2d and 10Pn-3d groups and the second one for presenting the results in the Unprimed group.

| **End point values** | Unprimed group | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 60 | | | |
| Units: Subjects | | | | |
| Anti-1 at PRE (N= 60) | 34 | | | |
| Anti-1 at Day 7 (N= 60) | 60 | | | |
| Anti-1 at Month 3 (N= 60) | 60 | | | |
| Anti-4 at PRE (N= 60) | 9 | | | |
| Anti-4 at Day 7 (N= 60) | 60 | | | |
| Anti-4 at Month 3 (N= 60) | 60 | | | |
| Anti-5 at PRE (N= 60) | 37 | | | |
| Anti-5 at Day 7 (N= 60) | 60 | | | |
| Anti-5 at Month 3 (N= 60) | 60 | | | |
| Anti-6B at PRE (N= 60) | 40 | | | |
| Anti-6B at Day 7 (N= 58) | 49 | | | |
| Anti-6B at Month 3 (N= 60) | 60 | | | |
| Anti-7F at PRE (N= 60) | 29 | | | |
| Anti-7F at Day 7 (N= 60) | 60 | | | |
| Anti-7F at Month 3 (N= 60) | 60 | | | |
| Anti-9V at PRE (N= 60) | 21 | | | |
| Anti-9V at Day 7 (N= 60) | 58 | | | |
| Anti-9V at Month 3 (N= 60) | 60 | | | |
| Anti-14 at PRE (N= 60) | 56 | | | |
| Anti-14 at Day 7 (N= 60) | 58 | | | |
| Anti-14 at Month 3 (N= 60) | 60 | | | |
| Anti-18C at PRE (N= 60) | 23 | | | |
| Anti-18C at Day 7 (N= 59) | 59 | | | |
| Anti-18C at Month 3 (N= 60) | 60 | | | |
| Anti-19F at PRE (N= 60) | 44 | | | |
| Anti-19F at Day 7 (N= 59) | 59 | | | |
| Anti-19F at Month 3 (N= 60) | 60 | | | |
| Anti-23F at PRE (N= 60) | 23 | | | |
| Anti-23F at Day 7 (N= 60) | 39 | | | |
| Anti-23F at Month 3 (N= 60) | 60 | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with Anti-pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F antibody concentrations ≥ 0.20 µg/mL in the 10Pn-2d and 10Pn-3d groups

| End point title | Number of subjects with Anti-pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F antibody concentrations ≥ 0.20 µg/mL in the 10Pn-2d and 10Pn-3d groups[7] |
|---|---|

End point description:

Antibodies assessed for this outcome measure were those against the vaccine pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C,19F and 23F (ANTI-1, -4, -5, -6B, -7F, -9V, -14, -18C, -19F and -23F). Antibody concentrations were measured by 22F enzyme-linked immunosorbent assay (ELISA), expressed as geometric mean concentrations (GMCs), in micrograms per milliliter (µg/mL). The seropositivity cut-off of the assay was an antibody concentration ≥ 0.05 µg/mL.

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

End point timeframe:

1 month after booster dose (Month 10) –in primary study 105539), pre-additional dose at Month 34 in the current study (Month 34) and one week after vaccination at Mont 34+7 days (Mth34+D7)

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: When time frames are not the same for the 3 groups for a same endpoint, the endpoint has been duplicated: the first one for presenting results in the 10Pn-2d and 10Pn-3d groups and the second one for presenting the results in the Unprimed group.

| **End point values** | 10Pn-2d group | 10Pn-3d group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 50 | 57 | | |
| Units: Subjects | | | | |
| Anti-1 at Month 10(N=50,57) | 50 | 57 | | |
| Anti-1 at Month 34(N=49,57) | 16 | 28 | | |
| Anti-1 at Mth34+D7(N=50,55) | 50 | 55 | | |
| Anti-4 at Month 10(N=50,57) | 50 | 57 | | |
| Anti-4 at Month 34(N=48,54) | 12 | 20 | | |
| Anti-4 at Mth34+D7(N=49,55) | 49 | 55 | | |
| Anti-5 at Month 10(N=50,57) | 50 | 57 | | |
| Anti-5 at Month 34(N=50,57) | 31 | 35 | | |
| Anti-5 at Mth34+D7(N=50,55) | 50 | 55 | | |
| Anti-6B at Month 10 (N=50,57) | 44 | 54 | | |
| Anti-6B at Month 34(N=48,57) | 29 | 44 | | |
| Anti-6B at Mth34+D7(N=50,55) | 49 | 55 | | |
| Anti-7F at Month 10(N=50,57) | 50 | 57 | | |
| Anti-7F at Month 34(N=49,56) | 37 | 53 | | |
| Anti-7F at Mth34+D7(N=50,55) | 50 | 55 | | |
| Anti-9V at Month 10(N=50,57) | 49 | 57 | | |
| Anti-9V at Month 34(N=50,57 | 27 | 45 | | |

| | | | | |
|---|---|---|---|---|
| Anti-9V at Mth34+D7(N=50,55) | 50 | 55 | | |
| Anti-14 at Month 10(N=50,57) | 50 | 57 | | |
| Anti-14 at Month 34(N=50,56) | 37 | 49 | | |
| Anti-14 at Mth34+D7(N=50,55) | 50 | 55 | | |
| Anti-18C at Month 1(N=50,57) | 50 | 56 | | |
| Anti-18C at Month 34(N=50, 56) | 35 | 44 | | |
| Anti-18C at Mth34+D7(N=50,55) | 50 | 55 | | |
| Anti-19F at Month 10(N=50,57) | 49 | 56 | | |
| Anti-19F at Month 34(N=47,56) | 39 | 47 | | |
| Anti-19F at Mth34+D7(N=50,55) | 50 | 55 | | |
| Anti-23F at Month 10(N=50,57) | 47 | 55 | | |
| Anti-23F at Month 34(N=49,56) | 29 | 36 | | |
| Anti-23F at Mth34+D7(N=50,55) | 49 | 55 | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with Anti-pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F antibody concentrations ≥ 0.20 µg/mL in the Unprimed group

| | |
|---|---|
| End point title | Number of subjects with Anti-pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F antibody concentrations ≥ 0.20 µg/mL in the Unprimed group[8] |

End point description:

Antibodies assessed for this outcome measure were those against the vaccine pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C,19F and 23F (ANTI-1, -4, -5, -6B, -7F, -9V, -14, -18C, -19F and -23F). Antibody concentrations were measured by 22F enzyme-linked immunosorbent assay (ELISA), expressed as geometric mean concentrations (GMCs), in micrograms per milliliter (µg/mL). The seropositivity cut-off of the assay was an antibody concentration ≥ 0.05 µg/mL.

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

End point timeframe:

Pre-vaccination (PRE), one week after dose 1 (Day 7) and one month after dose 2 (Month 3)

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: When time frames are not the same for the 3 groups for a same endpoint, the endpoint has been duplicated: the first one for presenting results in the 10Pn-2d and 10Pn-3d groups and the second one for presenting the results in the Unprimed group.

| End point values | Unprimed group | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 60 | | | |
| Units: Subjects | | | | |
| Anti-1 at PRE (N= 60) | 10 | | | |
| Anti-1 at Day 7 (N= 60) | 54 | | | |
| Anti-1 at Month 3 (N= 60) | 60 | | | |
| Anti-4 at PRE (N= 60) | 4 | | | |
| Anti-4 at Day 7 (N= 60) | 60 | | | |
| Anti-4 at Month 3 (N= 60) | 60 | | | |
| Anti-5 at PRE (N= 60) | 9 | | | |
| Anti-5 at Day 7 (N= 60) | 47 | | | |

| | | | | |
|---|---|---|---|---|
| Anti-5 at Month 3 (N= 60) | 60 | | | |
| Anti-6B at PRE (N= 60) | 19 | | | |
| Anti-6B at Day 7 (N= 58) | 29 | | | |
| Anti-6B at Month 3 (N= 60) | 56 | | | |
| Anti-7F at PRE (N= 60) | 11 | | | |
| Anti-7F at Day 7 (N= 60) | 54 | | | |
| Anti-7F at Month 3 (N= 60) | 60 | | | |
| Anti-9V at PRE (N= 60) | 7 | | | |
| Anti-9V at Day 7 (N= 60) | 40 | | | |
| Anti-9V at Month 3 (N= 60) | 60 | | | |
| Anti-14 at PRE (N= 60) | 27 | | | |
| Anti-14 at Day 7 (N= 60) | 42 | | | |
| Anti-14 at Month 3 (N= 60) | 60 | | | |
| Anti-18C at PRE (N= 60) | 8 | | | |
| Anti-18C at Day 7 (N= 59) | 56 | | | |
| Anti-18C at Month 3 (N= 60) | 60 | | | |
| Anti-19F at PRE (N= 60) | 29 | | | |
| Anti-19F at Day 7 (N= 59) | 57 | | | |
| Anti-19F at Month 3 (N= 60) | 60 | | | |
| Anti-23F at PRE (N= 60) | 11 | | | |
| Anti-23F at Day 7 (N= 60) | 16 | | | |
| Anti-23F at Month 3 (N= 60) | 56 | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Titers for opsonophagocytic activity against vaccine pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F in the 10Pn-2d and 10Pn-3d groups

| | |
|---|---|
| End point title | Titers for opsonophagocytic activity against vaccine pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F in the 10Pn-2d and 10Pn-3d groups[9] |

End point description:

Seropositivity status defined as Opsonophacocytic activity against pneumococcal serotypes ≥ 8.

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

End point timeframe:

1 month after booster dose (Month 10) –in primary study 105539), pre-additional dose at Month 34 in the current study (Month 34) and one week after vaccination at Mont 34+7 days (Mth34+D7)

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: When time frames are not the same for the 3 groups for a same endpoint, the endpoint has been duplicated: the first one for presenting results in the 10Pn-2d and 10Pn-3d groups and the second one for presenting the results in the Unprimed group.

| **End point values** | 10Pn-2d group | 10Pn-3d group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 48 | 55 | | |
| Units: Titers | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Opsono-1 at Month 10(N=44,53) | 243.9 (137.3 to 433.3) | 176.9 (104 to 301) | | |
| Opsono-1 at Month 34 N=47,55) | 5.5 (4.3 to 7) | 6.2 (4.9 to 8) | | |
| Opsono-1 at Mth34+D7(N=48,55) | 2342.2 (1788.8 to 3066.7) | 2321.5 (1827.1 to 2949.7) | | |
| Opsono-4 at Month 10(N=43,51) | 937.6 (600.8 to 1463.4) | 1347 (1068.8 to 1697.7) | | |
| Opsono-4 at Month 34(N=44,52) | 9.6 (4.9 to 18.8) | 9.5 (5.8 to 15.6) | | |
| Opsono-4 at Mth34+D7(N=48,53) | 13247.5 (9898 to 17730.4) | 17732.6 (13218.8 to 23787.7) | | |
| Opsono-5 at Month 10(N=45,54) | 154 (94.2 to 251.6) | 181.2 (125.4 to 262) | | |
| Opsono-5 at Month 34(N=47,54) | 6.7 (5.2 to 8.6) | 8 (6.1 to 10.6) | | |
| Opsono-5 at Mth34+D7(N=48,55) | 991.5 (769.8 to 1277.1) | 1221.1 (912.4 to 1634.2) | | |
| Opsono-6B at Month 10(N=44,51) | 292.2 (147.1 to 580.3) | 458.8 (254.8 to 825.9) | | |
| Opsono-6B at Month 34(N=42,54) | 61.5 (22.8 to 165.6) | 126.3 (59.4 to 268.5) | | |
| Opsono-6B at Mth34+D7(N=47,54) | 3312.9 (1751.2 to 6267.2) | 3136 (1730 to 5684.6) | | |
| Opsono-7F at Month 10(N=44,53) | 2257.8 (1601.9 to 3182.3) | 3856.8 (2890.4 to 5146.2) | | |
| Opsono-7F at Month 34(N=45,53) | 1329.1 (778.8 to 2268.4) | 1225.5 (842.5 to 1782.6) | | |
| Opsono-7F at Mth34+D7(N=48,52) | 20779 (14616.7 to 29539.1) | 22461.4 (16876.9 to 29893.7) | | |
| Opsono-9V at Month 10(N=44,54) | 1581.7 (1147.7 to 2179.9) | 2013.9 (1565.3 to 2591) | | |
| Opsono-9V at Month 34(N=43,53) | 307.4 (210.3 to 449.4) | 292.3 (221 to 386.6) | | |
| Opsono-9V at Mth34+D7(N=48,52 | 21193.6 (16100.3 to 27898.2) | 19038.4 (14154.7 to 25607.2) | | |
| Opsono-14 at Month 10(N=35,52) | 1092.5 (691.9 to 1725) | 1207.1 (961.4 to 1515.5) | | |
| Opsono-14 at Month 34(N=41,49) | 421.5 (258.8 to 686.5) | 738.6 (540 to 1010.2) | | |
| Opsono-14 at Mth34+D7(N=48,54) | 14310 (10214 to 20048.7) | 14670.9 (10258 to 20982.2) | | |
| Opsono-18C at Month 10(N=45,54) | 375.8 (251.3 to 562.1) | 567.4 (422.8 to 761.5) | | |
| Opsono-18C at Month 34(N=45,54) | 11 (6 to 20.2) | 17.7 (9.6 to 32.9) | | |
| Opsono-18C at Mth34+D7(N=48,51) | 6095.8 (4090.7 to 9083.8) | 6448.7 (4258.7 to 9764.9) | | |

| | | | | |
|---|---|---|---|---|
| Opsono-19F at Month 10(N=43,54) | 463.7 (318.3 to 675.6) | 950.5 (653.3 to 1383) | | |
| Opsono-19F at Month 34(N= 47,55) | 34.1 (18.4 to 63.2) | 48.4 (25.9 to 90.6) | | |
| Opsono-19F at Mth34+D7(N=48,55) | 2231.5 (1267.7 to 3927.9) | 5684.4 (3647.8 to 8858) | | |
| Opsono-23F at Month 10(N=45,53) | 1414.6 (827.9 to 2417.1) | 1984.8 (1520.3 to 2591.3) | | |
| Opsono-23F at Month 34(N=43,49) | 458.5 (186.3 to 1128.2) | 465.6 (209.6 to 1034) | | |
| Opsono-23F at Mth34+D7(N=48,54) | 15688.3 (10571.2 to 23282.4) | 13812.6 (9566 to 19944.4) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Titers for opsonophagocytic activity against vaccine pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F in the Unprimed group

| | |
|---|---|
| End point title | Titers for opsonophagocytic activity against vaccine pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F in the Unprimed group[10] |

End point description:

Seropositivity status defined as Opsonophacocytic activity against pneumococcal serotypes ≥ 8.

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

End point timeframe:

Pre-vaccination (PRE), one week after dose 1 (Day 7) and one month after dose 2 (Month 3)

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: When time frames are not the same for the 3 groups for a same endpoint, the endpoint has been duplicated: the first one for presenting results in the 10Pn-2d and 10Pn-3d groups and the second one for presenting the results in the Unprimed group.

| **End point values** | Unprimed group | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 59 | | | |
| Units: Titers | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Opsono-1 at PRE (N= 58) | 4 (4 to 4) | | | |
| Opsono-1 at Day 7 (N= 58) | 441.1 (302.4 to 643.4) | | | |
| Opsono-1 at Month 3 (N= 56) | 103 (67.6 to 157) | | | |
| Opsono-4 at PRE (N= 58) | 5.1 (3.9 to 6.7) | | | |
| Opsono-4 at Day 7 (N= 58) | 9675.9 (7792.2 to 12014.9) | | | |
| Opsono-4 at Month 3 (N= 56) | 2687.5 (2165 to 3336.1) | | | |

| | | | | |
|---|---|---|---|---|
| Opsono-5 at PRE (N= 59 | 4.1 (3.9 to 4.5) | | | |
| Opsono-5 at Day 7 (N= 57) | 330 (200.5 to 543) | | | |
| Opsono-5 at Month 3 (N= 56) | 127.6 (92.7 to 175.6) | | | |
| Opsono-6B at PRE (N= 55) | 21.6 (11 to 42.4) | | | |
| Opsono-6B at Day 7 (N= 54) | 438.2 (208.4 to 921.5) | | | |
| Opsono-6B at Month 3 (N= 57) | 1040.9 (652.8 to 1659.5) | | | |
| Opsono-7F at PRE (N= 55) | 644.2 (355.5 to 1167.3) | | | |
| Opsono-7F at Day 7 (N=57) | 11048.4 (8626.3 to 14150.5) | | | |
| Opsono-7F at Month 3 (N= 55) | 6213.1 (4793.1 to 8053.7) | | | |
| Opsono-9V at PRE (N= 55) | 103.1 (53.8 to 197.6) | | | |
| Opsono-9V at Day 7 (N= 57) | 12217.8 (9359.1 to 15949.8) | | | |
| Opsono-9V at Month 3 (N= 55) | 6085.2 (4718.5 to 7847.9) | | | |
| Opsono-14 at PRE (N= 53) | 252.5 (138.1 to 461.5) | | | |
| Opsono-14 at Day 7 (N= 57) | 3948.7 (2958.9 to 5269.5) | | | |
| Opsono-14 at Month 3 (N= 56) | 4978.9 (3857.8 to 6425.9) | | | |
| Opsono-18C at PRE (N= 48) | 6.1 (4 to 9.3) | | | |
| Opsono-18C at Day 7 (N= 57) | 3905.6 (2648 to 5760.4) | | | |
| Opsono-18C at Month 3 (N= 56) | 3984.5 (3187.9 to 4980.2) | | | |
| Opsono-19F at PRE (N= 59) | 8.4 (5.6 to 12.7) | | | |
| Opsono-19F at Day 7 (N= 57) | 367.5 (202.7 to 666.5) | | | |
| Opsono-19F at Month 3 (N= 56) | 1772.5 (1285.9 to 2443.3) | | | |
| Opsono-23F at PRE (N= 52) | 265.3 (121.5 to 579.6) | | | |
| Opsono-23F at Day 7 (N= 58) | 5059 (3800.6 to 6734) | | | |
| Opsono-23F at Month 3 (N= 57) | 5095.5 (3992.3 to 6503.6) | | | |

**Statistical analyses**

No statistical analyses for this end point

## Secondary: Antibody Geometric Mean Concentrations (GMCs) against the vaccine pneumococcal serotypes 6A and 19A in the 10Pn-2d and 10Pn-3d groups

| End point title | Antibody Geometric Mean Concentrations (GMCs) against the vaccine pneumococcal serotypes 6A and 19A in the 10Pn-2d and 10Pn-3d groups[11] |
|---|---|

End point description:

Antibodies assessed for this outcome measure were those against the vaccine pneumococcal serotypes 6A and19A (ANTI-6A and19A). Antibody concentrations were measured by 22F enzyme-linked immunosorbent assay (ELISA), expressed as geometric mean concentrations (GMCs), in micrograms per milliliter (µg/mL). The seropositivity cut-off of the assay was an antibody concentration ≥ 0.05 µg/mL.

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

End point timeframe:

1 month after booster dose (Month 10) –in primary study 105539), pre-additional dose at Month 34 in the current study (Month 34) and one week after vaccination at Mont 34+7 days (Mth34+D7)

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: When time frames are not the same for the 3 groups for a same endpoint, the endpoint has been duplicated: the first one for presenting results in the 10Pn-2d and 10Pn-3d groups and the second one for presenting the results in the Unprimed group.

| **End point values** | 10Pn-2d group | 10Pn-3d group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 50 | 57 | | |
| Units: µg/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-6A at Month 10 (N= 49, 57) | 0.31 (0.2 to 0.48) | 0.51 (0.33 to 0.77) | | |
| Anti-6A at Month 34 (N= 48, 55) | 0.26 (0.16 to 0.42) | 0.45 (0.28 to 0.71) | | |
| Anti-6A at Mth34+D7 (N= 50, 55) | 1.13 (0.71 to 1.79) | 2 (1.32 to 3.03) | | |
| Anti-19A at Month 10 (N= 50, 57) | 0.8 (0.53 to 1.2) | 0.75 (0.5 to 1.12) | | |
| Anti-19A at Month 34 (N= 49, 57) | 0.31 (0.2 to 0.49) | 0.26 (0.17 to 0.4) | | |
| Anti-19A at Mth34+D7 (N= 50, 55) | 3.44 (2.3 to 5.15) | 3.76 (2.47 to 5.73) | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Antibody Geometric Mean Concentrations (GMCs) against the vaccine pneumococcal serotypes 6A and 19A in the Unprimed group

| End point title | Antibody Geometric Mean Concentrations (GMCs) against the vaccine pneumococcal serotypes 6A and 19A in the Unprimed group[12] |
|---|---|

End point description:

Antibodies assessed for this outcome measure were those against the vaccine pneumococcal serotypes 6A and 19A (ANTI-6A and 19A). Antibody concentrations were measured by 22F enzyme-linked

immunosorbent assay (ELISA), expressed as geometric mean concentrations (GMCs), in micrograms per milliliter (µg/mL). The seropositivity cut-off of the assay was an antibody concentration ≥ 0.05 µg/mL.

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

End point timeframe:

Pre-vaccination (PRE), one week after dose 1 (Day 7) and one month after dose 2 (Month 3)

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: When time frames are not the same for the 3 groups for a same endpoint, the endpoint has been duplicated: the first one for presenting results in the 10Pn-2d and 10Pn-3d groups and the second one for presenting the results in the Unprimed group.

| **End point values** | Unprimed group | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 60 | | | |
| Units: µg/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-6A at PRE (N= 60) | 0.11 (0.08 to 0.16) | | | |
| Anti-6A at Day 7 (N= 60) | 0.15 (0.11 to 0.21) | | | |
| Anti-6A at Month 3 (N= 60) | 0.58 (0.42 to 0.79) | | | |
| Anti-19A at PRE (N= 60) | 0.13 (0.09 to 0.2) | | | |
| Anti-19A at Day 7 (N= 59) | 0.32 (0.21 to 0.49) | | | |
| Anti-19A at Month 3 (N= 60) | 1.97 (1.46 to 2.65) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with Anti-pneumococcal serotypes 6A and 19A antibody concentrations ≥ 0.05 µg/mL in the 10Pn-2d and 10Pn-3d groups

| End point title | Number of subjects with Anti-pneumococcal serotypes 6A and 19A antibody concentrations ≥ 0.05 µg/mL in the 10Pn-2d and 10Pn-3d groups[13] |
|---|---|

End point description:

Antibodies assessed for this outcome measure were those against the vaccine pneumococcal serotypes 6A and 19A (ANTI-6A and 19A). Antibody concentrations were measured by 22F enzyme-linked immunosorbent assay (ELISA), expressed as geometric mean concentrations (GMCs), in micrograms per milliliter (µg/mL). The seropositivity cut-off of the assay was an antibody concentration ≥ 0.05 µg/mL.

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

End point timeframe:

1 month after booster dose (Month 10) –in primary study 105539), pre-additional dose at Month 34 in the current study (Month 34) and one week after vaccination at Mont 34+7 days (Mth34+D7)

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: When time frames are not the same for the 3 groups for a same endpoint, the endpoint has been duplicated: the first one for presenting results in the 10Pn-2d and 10Pn-3d groups and the

second one for presenting the results in the Unprimed group.

| End point values | 10Pn-2d group | 10Pn-3d group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 50 | 57 | | |
| Units: Subjects | | | | |
| Anti-6A at Month 10 (N= 49, 57) | 42 | 51 | | |
| Anti-6A at Month 34 (N= 48, 55) | 43 | 51 | | |
| Anti-6A at Mth34+D7 (N= 50, 55) | 48 | 55 | | |
| Anti-19A at Month 10 (N= 50, 57) | 48 | 54 | | |
| Anti-19A at Month 34 (N= 49, 57) | 44 | 50 | | |
| Anti-19A at Mth34+D7 (N= 50, 55) | 50 | 55 | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with Anti-pneumococcal serotypes 6A and19A antibody concentrations ≥ 0.05 µg/mL in the Unprimed group

| End point title | Number of subjects with Anti-pneumococcal serotypes 6A and19A antibody concentrations ≥ 0.05 µg/mL in the Unprimed group[14] |
|---|---|

End point description:

Antibodies assessed for this outcome measure were those against the vaccine pneumococcal serotypes 6A and 19A (ANTI-6A and 19A). Antibody concentrations were measured by 22F enzyme-linked immunosorbent assay (ELISA), expressed as geometric mean concentrations (GMCs), in micrograms per milliliter (µg/mL). The seropositivity cut-off of the assay was an antibody concentration ≥ 0.05 µg/mL.

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

End point timeframe:

Pre-vaccination (PRE), one week after dose 1 (Day 7) and one month after dose 2 (Month 3)

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: When time frames are not the same for the 3 groups for a same endpoint, the endpoint has been duplicated: the first one for presenting results in the 10Pn-2d and 10Pn-3d groups and the second one for presenting the results in the Unprimed group.

| End point values | Unprimed group | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 60 | | | |
| Units: Subjects | | | | |
| Anti-6A at PRE (N= 60) | 47 | | | |
| Anti-6A at Day 7 (N= 60) | 50 | | | |
| Anti-6A at Month 3 (N= 60) | 59 | | | |
| Anti-19A at PRE (N= 60) | 41 | | | |
| Anti-19A at Day 7 (N= 59) | 55 | | | |
| Anti-19A at Month 3 (N= 60) | 60 | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with Anti-pneumococcal serotypes 6A and 19A antibody concentrations ≥ 0.20 µg/mL in the 10Pn-2d and 10Pn-3d groups

| End point title | Number of subjects with Anti-pneumococcal serotypes 6A and 19A antibody concentrations ≥ 0.20 µg/mL in the 10Pn-2d and 10Pn-3d groups[15] |
|---|---|

End point description:

Antibodies assessed for this outcome measure were those against the vaccine pneumococcal serotypes 6A and 19A (ANTI-6A and 19A). Antibody concentrations were measured by 22F enzyme-linked immunosorbent assay (ELISA), expressed as geometric mean concentrations (GMCs), in micrograms per milliliter (µg/mL). The seropositivity cut-off of the assay was an antibody concentration ≥ 0.05 µg/mL.

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

End point timeframe:

1 month after booster dose (Month 10) –in primary study 105539), pre-additional dose at Month 34 in the current study (Month 34) and one week after vaccination at Mont 34+7 days (Mth34+D7)

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: When time frames are not the same for the 3 groups for a same endpoint, the endpoint has been duplicated: the first one for presenting results in the 10Pn-2d and 10Pn-3d groups and the second one for presenting the results in the Unprimed group.

| **End point values** | 10Pn-2d group | 10Pn-3d group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 50 | 57 | | |
| Units: Subjects | | | | |
| Anti-6A at Month 10 (N= 49, 57) | 31 | 43 | | |
| Anti-6A at Month 34 (N= 48, 55) | 22 | 38 | | |
| Anti-6A at Mth34+D7 (N= 50, 55) | 44 | 51 | | |
| Anti-19A at Month 10 (N= 50, 57) | 41 | 45 | | |
| Anti-19A at Month 34 (N= 49, 57) | 26 | 30 | | |
| Anti-19A at Mth34+D7 (N= 50, 55) | 47 | 54 | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with Anti-pneumococcal serotypes 6A and19A antibody concentrations ≥ 0.20 µg/mL in the Unprimed group

| End point title | Number of subjects with Anti-pneumococcal serotypes 6A and19A antibody concentrations ≥ 0.20 µg/mL in the Unprimed group[16] |
|---|---|

End point description:

Antibodies assessed for this outcome measure were those against the vaccine pneumococcal serotypes 6A and 19A (ANTI-6A and 19A). Antibody concentrations were measured by 22F enzyme-linked immunosorbent assay (ELISA), expressed as geometric mean concentrations (GMCs), in micrograms per milliliter (µg/mL). The seropositivity cut-off of the assay was an antibody concentration ≥ 0.05 µg/mL.

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

End point timeframe:

Pre-vaccination (PRE), one week after dose 1 (Day 7) and one month after dose 2 (Month 3)

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: When time frames are not the same for the 3 groups for a same endpoint, the endpoint has been duplicated: the first one for presenting results in the 10Pn-2d and 10Pn-3d groups and the second one for presenting the results in the Unprimed group.

| **End point values** | Unprimed group | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 60 | | | |
| Units: Subjects | | | | |
| Anti-6A at PRE (N= 60) | 13 | | | |
| Anti-6A at Day 7 (N= 60) | 24 | | | |
| Anti-6A at Month 3 (N= 60) | 49 | | | |
| Anti-19A at PRE (N= 60) | 22 | | | |
| Anti-19A at Day 7 (N= 59) | 33 | | | |
| Anti-19A at Month 3 (N= 60) | 58 | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Titers for opsonophagocytic activity against vaccine pneumococcal serotypes 6A and 19A in the 10Pn-2d and 10Pn-3d groups

| End point title | Titers for opsonophagocytic activity against vaccine pneumococcal serotypes 6A and 19A in the 10Pn-2d and 10Pn-3d groups[17] |
|---|---|

End point description:

Seropositivity status defined as Opsonophacocytic activity against pneumococcal serotypes ≥ 8

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

End point timeframe:

1 month after booster dose (Month 10) –in primary study 105539), pre-additional dose at Month 34 in the current study (Month 34) and one week after vaccination at Mont 34+7 days (Mth34+D7)

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: When time frames are not the same for the 3 groups for a same endpoint, the endpoint has been duplicated: the first one for presenting results in the 10Pn-2d and 10Pn-3d groups and the second one for presenting the results in the Unprimed group.

| End point values | 10Pn-2d group | 10Pn-3d group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 48 | 55 | | |
| Units: Titers | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Opsono-6A at Month 10 (N= 35, 44) | 60.9 (25.9 to 143.1) | 135 (68.3 to 267) | | |
| Opsono-6A at Month 34 (N= 40, 47) | 64.3 (27.1 to 152.7) | 81.5 (39.7 to 167.5) | | |
| Opsono-6A at Mth34+D7 (N= 45, 50) | 1639.4 (958.6 to 2803.9) | 1267.3 (713.8 to 2250) | | |
| Opsono-19A at Month 10 (N= 36, 46) | 14.4 (7.6 to 27.3) | 35.9 (18 to 71.6) | | |
| Opsono-19A at Month 34 (N= 45, 55) | 8 (5.2 to 12.2) | 8.6 (5.6 to 13.4) | | |
| Opsono-19A at Mth34+D7 (N= 48, 55) | 799.3 (372.8 to 1713.4) | 1871.6 (975.8 to 3589.8) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Titers for opsonophagocytic activity against vaccine pneumococcal serotypes 6A and 19A in the Unprimed group

| End point title | Titers for opsonophagocytic activity against vaccine pneumococcal serotypes 6A and 19A in the Unprimed group[18] |
|---|---|

End point description:

Seropositivity status defined as Opsonophacocytic activity against pneumococcal serotypes ≥ 8

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

End point timeframe:

Pre-vaccination (PRE), one week after dose 1 (Day 7) and one month after dose 2 (Month 3)

Notes:

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: When time frames are not the same for the 3 groups for a same endpoint, the endpoint has been duplicated: the first one for presenting results in the 10Pn-2d and 10Pn-3d groups and the second one for presenting the results in the Unprimed group.

| End point values | Unprimed group | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 58 | | | |
| Units: Titers | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Opsono-6A at PRE (N= 50) | 36.3 (18.9 to 69.6) | | | |
| Opsono-6A at Day 7 (N= 52) | 389.6 (215.2 to 705.5) | | | |
| Opsono-6A at Month 3 (N= 52) | 715.2 (487.3 to 1049.6) | | | |
| Opsono-19A at PRE (N= 58) | 5.4 (4.2 to 6.9) | | | |

| | | | | |
|---|---|---|---|---|
| Opsono-19A at Day 7 (N= 55) | 211.9 (99.9 to 449.7) | | | |
| Opsono-19A at Month 3 (N= 53) | 406.4 (227.3 to 726.9) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Concentrations of antibodies against protein D (ANTI-PD) in the 10Pn-2d and 10Pn-3d groups

| End point title | Concentrations of antibodies against protein D (ANTI-PD) in the 10Pn-2d and 10Pn-3d groups[19] |
|---|---|

End point description:

ANTI-PD concentrations are expressed as geometric mean concentrations (GMCs), in enzyme-linked immunosorbent assay (ELISA) unit per milliliter (EL.U/mL). Seropositivity status is defined as Anti-PD antibody concentrations ≥ 100 EL.U/mL.

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

End point timeframe:

1 month after booster dose (Month 10) –in primary study 105539), pre-additional dose at Month 34 in the current study (Month 34) and one week after vaccination at Mont 34+7 days (Mth34+D7)

Notes:

[19] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: When time frames are not the same for the 3 groups for a same endpoint, the endpoint has been duplicated: the first one for presenting results in the 10Pn-2d and 10Pn-3d groups and the second one for presenting the results in the Unprimed group.

| **End point values** | 10Pn-2d group | 10Pn-3d group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 50 | 57 | | |
| Units: EL.U/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-PD at Month 10 (N= 48, 56) | 1438 (1018.9 to 2029.4) | 2241.3 (1752.5 to 2866.3) | | |
| Anti-PD at Month 34 (N= 50, 57) | 301.6 (219.5 to 414.3) | 461.3 (351.1 to 606) | | |
| Anti-PD at Mth34+D7 (N= 50, 55) | 1724.1 (1299.4 to 2287.5) | 2113.2 (1651.2 to 2704.5) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Concentrations of antibodies against protein D (ANTI-PD) in the Unprimed group

| End point title | Concentrations of antibodies against protein D (ANTI-PD) in the Unprimed group[20] |
|---|---|

End point description:

ANTI-PD concentrations are expressed as geometric mean concentrations (GMCs), in enzyme-linked immunosorbent assay (ELISA) unit per milliliter (EL.U/mL). Seropositivity status is defined as Anti-PD antibody concentrations ≥ 100 EL.U/mL.

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

End point timeframe:

Pre-vaccination (PRE), one week after dose 1 (Day 7) and one month after dose 2 (Month 3)

Notes:

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: When time frames are not the same for the 3 groups for a same endpoint, the endpoint has been duplicated: the first one for presenting results in the 10Pn-2d and 10Pn-3d groups and the second one for presenting the results in the Unprimed group.

| **End point values** | Unprimed group | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 60 | | | |
| Units: EL.U/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-PD at PRE (N= 60) | 110.9 (88.8 to 138.6) | | | |
| Anti-PD at Day 7 (N= 60) | 536.3 (390.7 to 736.2) | | | |
| Anti-PD at Month 3 (N= 60) | 960.4 (752.7 to 1225.5) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with B-cells detection in the 10Pn-2d and 10Pn-3d groups

| End point title | Number of subjects with B-cells detection in the 10Pn-2d and 10Pn-3d groups[21] |
|---|---|

End point description:

Quantification of memory B-cells that produce antibodies against vaccine pneumococcal serotypes (PS) 6B, 18C, 19F, 23F and C-PS (Elispot assay), prior to, and 7-10 days post- additional dose. Since none of the blood samples for memory B-cell quantification taken at the Slovakian site were suitable for testing, the assay for memory B-cell quantification was only performed on blood samples from all other evaluable subjects.

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

End point timeframe:

pre-additional dose at Month 34 in the current study (Month 34) and one week after vaccination at Mont 34+7 days (Mth34+D7)

Notes:

[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: When time frames are not the same for the 3 groups for a same endpoint, the endpoint has been duplicated: the first one for presenting results in the 10Pn-2d and 10Pn-3d groups and the second one for presenting the results in the Unprimed group.

| End point values | 10Pn-2d group | 10Pn-3d group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 10 | 13 | | |
| Units: Subjects | | | | |
| arithmetic mean (standard deviation) | | | | |
| 18C PS at Month 34 (N=10,11) | 377 (± 459.3) | 424.9 (± 668.2) | | |
| 18C PS at Mth34+D7 (N= 7,13) | 1205.3 (± 661.4) | 2891.2 (± 2274.5) | | |
| 19F PS at Month 34 (N= 10,11) | 163.1 (± 306.4) | 635.4 (± 1196.6) | | |
| 19F PS at Mth34+D7 (N= 7,13) | 856.7 (± 1211.7) | 1626 (± 1760.5) | | |
| 23F PS at Month 34 (N= 10,11) | 174.2 (± 285) | 212.2 (± 320.8) | | |
| 23F PS at Mth34+D7 (N= 7,13) | 120.1 (± 92) | 351.9 (± 400.4) | | |
| 6B PS at Month 34 (N= 10,11) | 136.1 (± 131.8) | 508.5 (± 606.3) | | |
| 6B PS at Mth34+D7 (N= 7,13) | 153.1 (± 216) | 469.7 (± 554.5) | | |
| C-PS at Month 34 (N= 10,11) | 246.3 (± 247.3) | 751.2 (± 790.5) | | |
| C-PS at Mth34+D7 (N= 7,13) | 167.6 (± 92) | 600.5 (± 488.8) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with any and Grade 3 solicited local symptoms

| End point title | Number of subjects with any and Grade 3 solicited local symptoms |
|---|---|

End point description:

Assessed local symptoms were pain, redness and swelling. Any = Occurrence of the specified solicited local symptom, regardless of intensity. Grade 3 Pain = Crying when limb was moved/spontaneously painful. Grade 3 Redness/Swelling = Redness/swelling at injection site larger than (>) 30 millimeters (mm).

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

End point timeframe:

during the 4-day (Days 0-3)post-vaccination period with the 10Pn-PD-DiT vaccine, following the additional dose in the 10Pn-2d and the 10Pn-3d groups and across the 2 doses in the Unprimed group

| End point values | 10Pn-2d group | 10Pn-3d group | Unprimed group | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 51 | 59 | 62 | |
| Units: Subjects | | | | |
| Any Pain (N=51, 59, 62) | 41 | 44 | 49 | |
| Grade 3 Pain (N=51, 59, 62) | 3 | 4 | 6 | |
| Any Redness (N=51, 59, 62) | 34 | 35 | 41 | |

| | | | | |
|---|---|---|---|---|
| Grade 3 Redness (N=51, 59, 62) | 9 | 12 | 15 | |
| Any Swelling (N=51, 59, 62) | 28 | 27 | 30 | |
| Grade 3 Swelling (N=51, 59, 62) | 5 | 9 | 9 | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number/percentage of subjects with any, Grade 3 and Related solicited general symptoms

| End point title | Number/percentage of subjects with any, Grade 3 and Related solicited general symptoms |
|---|---|

End point description:

Assessed solicited general symptoms were Drowsiness, Irritability/Fussiness (Irr./Fuss.), Loss of appetite (Loss Appet.) and Fever (rectal temperature higher than [≥] 38.0 degrees Celsius [°C]),. Any = Occurrence of the specified solicited general symptom, regardless of intensity or relationship to vaccination. Related = Occurrence of the specified symptom assessed by the investigators as causally related to vaccination. Grade 3 Drowsiness = Drowsiness that prevented normal everyday activities. Grade 3 Irr./Fuss. = Crying that could not be comforted/prevented normal everyday activities. Grade 3 Loss of appetite = Subject did not eat at all. Grade 3 Fever = Rectal temperature higher than (>) 40.0°C.

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

End point timeframe:

during the 4-day (Days 0-3)post-vaccination period with the 10Pn-PD-DiT vaccine, following the additional dose in the 10Pn-2d and the 10Pn-3d groups and across the 2 doses in the Unprimed group.

| **End point values** | 10Pn-2d group | 10Pn-3d group | Unprimed group | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 51 | 59 | 62 | |
| Units: Subjects | | | | |
| Any Drowsiness (N=51, 59, 62) | 20 | 23 | 17 | |
| Grade 3 Drowsiness (N=51, 59, 62) | 0 | 0 | 0 | |
| Related Drowsiness (N=51, 59, 62) | 20 | 23 | 17 | |
| Any Fever (N=51, 59, 62) | 9 | 5 | 8 | |
| Grade 3 Fever (N=51, 59, 62) | 0 | 0 | 0 | |
| Related Fever (N=51, 59, 62) | 9 | 4 | 7 | |
| Any Irr./Fuss (N=51, 59, 62) | 20 | 27 | 21 | |
| Grade 3 Irr./Fuss. (N=51, 59, 62) | 0 | 0 | 0 | |
| Related Irr./Fuss. (N=51, 59, 62) | 20 | 25 | 20 | |
| Any Loss Appet. (N=51, 59, 62) | 12 | 13 | 14 | |
| Grade 3 Loss Appet. (N=51, 59, 62) | 0 | 0 | 0 | |
| Related Loss Appet. (N=51, 59, 62) | 12 | 13 | 14 | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number (%) of subjects with unsolicited adverse events

| End point title | Number (%) of subjects with unsolicited adverse events |
|---|---|

End point description:

An unsolicited AE was defined as any untoward medical occurrence in a clinical investigation subject, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. An AE can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a medicinal product. For the marketed products administered in the study, this also included failure to produce expected benefits (i.e. lack of efficacy), abuse or misuse of the product. Any = Occurrence of an unsolicited AE, regardless of intensity or relationship to vaccination.

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

End point timeframe:

Within the 31-day (Days 0-30) period post vaccination, with the 10Pn-PD-DiT vaccine, following the additional dose in the 10Pn-2d and the 10Pn-3d groups and across the 2 doses in the Unprimed group

| **End point values** | 10Pn-2d group | 10Pn-3d group | Unprimed group | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 51 | 59 | 62 | |
| Units: Subjects | | | | |
| Any AE | 24 | 24 | 40 | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number (%) of subjects with serious adverse events

| End point title | Number (%) of subjects with serious adverse events |
|---|---|

End point description:

A SAE was defined as any medical occurrence that resulted in death, was life-threatening, required hospitalization or prolongation of hospitalization, resulted in disability/incapacity in a subject. AE(s) considered as SAE(s) also included invasive or malignant cancers, intensive treatment in an emergency room or at home for allergic bronchospasm, blood dyscrasias or convulsions that did not result in hospitalisation, as per the medical or scientific judgement of the physician. Any = Occurrence of a SAE, regardless of relationship to vaccination.

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

End point timeframe:

During the 31-day period following vaccination period

| End point values | 10Pn-2d group | 10Pn-3d group | Unprimed group | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 51 | 59 | 62 | |
| Units: Subjects | | | | |
| Any SAE | 1 | 1 | 1 | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with B-cells detection in the Unprimed group

| End point title | Number of subjects with B-cells detection in the Unprimed group[22] |
|---|---|

End point description:

Quantification of memory B-cells that produce antibodies against vaccine pneumococcal serotypes (PS) 6B, 18C, 19F, 23F and C-PS (Elispot assay), prior to, and 7-10 days post-dose 1. Since none of the blood samples for memory B-cell quantification taken at the Slovakian site were suitable for testing, the assay for memory B-cell quantification was only performed on blood samples from all other evaluable subjects.

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

End point timeframe:

Pre-vaccination (PRE), one week after dose 1 (Day 7)

Notes:

[22] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: When time frames are not the same for the 3 groups for a same endpoint, the endpoint has been duplicated: the first one for presenting results in the 10Pn-2d and 10Pn-3d groups and the second one for presenting the results in the Unprimed group.

| End point values | Unprimed group | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 13 | | | |
| Units: Subjects | | | | |
| arithmetic mean (standard deviation) | | | | |
| 18C PS at PRE (N= 12) | 246.5 (± 310.8) | | | |
| 18C PS at Day 7 (N= 13) | 3014.2 (± 4168.4) | | | |
| 19F PS at PRE (N= 12) | 306.4 (± 423.1) | | | |
| 19F PS at Day 7 (N= 13) | 599.8 (± 643.8) | | | |
| 23F PS at PRE (N= 12) | 280 (± 492.2) | | | |
| 23F PS at Day 7 (N= 13) | 450 (± 529.4) | | | |
| 6B PS at PRE (N= 12) | 159.8 (± 220.7) | | | |
| 6B PS at Day 7 (N= 13) | 432.4 (± 478.3) | | | |
| C-PS at PRE (N= 12) | 751.9 (± 463) | | | |
| C-PS at Day 7 (N= 13) | 789.2 (± 751.1) | | | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Solicited symptoms during the 4-day post-vaccination period and Unsolicited AEs & SAEs: during the 31-day post-vaccination period, following additional dose in the 10Pn-2d and the 10Pn-3d groups and across the 2 doses in the Unprimed group.

Adverse event reporting additional description:

Occurrences (all and "related to the treatment") were not calculated during the analysis and are filled in with "subjects affected" similar information.

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

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 12.1 |

### Reporting groups

| | |
|---|---|
| Reporting group title | 10Pn-2d Group |
| Reporting group description: - | |
| Reporting group title | 10Pn-3d Group |
| Reporting group description: - | |
| Reporting group title | Unprimed Group |

Reporting group description: -

| Serious adverse events | 10Pn-2d Group | 10Pn-3d Group | Unprimed Group |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 1 / 59 (1.69%) | 1 / 62 (1.61%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | | | |
| Gastrointestinal disorders | | | |
| Gastritis | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 59 (0.00%) | 0 / 62 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 59 (0.00%) | 1 / 62 (1.61%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyelonephritis | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 59 (1.69%) | 0 / 62 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

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

| **Non-serious adverse events** | 10Pn-2d Group | 10Pn-3d Group | Unprimed Group |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 41 / 51 (80.39%) | 44 / 59 (74.58%) | 49 / 62 (79.03%) |
| General disorders and administration site conditions | | | |
| Pain | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 41 / 51 (80.39%) | 44 / 59 (74.58%) | 49 / 62 (79.03%) |
| occurrences (all) | 41 | 44 | 49 |
| Redness | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 34 / 51 (66.67%) | 35 / 59 (59.32%) | 41 / 62 (66.13%) |
| occurrences (all) | 34 | 35 | 41 |
| Swelling | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 28 / 51 (54.90%) | 27 / 59 (45.76%) | 30 / 62 (48.39%) |
| occurrences (all) | 28 | 27 | 30 |
| Drowsiness | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 20 / 51 (39.22%) | 23 / 59 (38.98%) | 17 / 62 (27.42%) |
| occurrences (all) | 20 | 23 | 17 |
| Fever (Rectally, ≥ 38.0°C) | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 9 / 51 (17.65%) | 5 / 59 (8.47%) | 8 / 62 (12.90%) |
| occurrences (all) | 9 | 5 | 8 |
| Irritability | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 20 / 51 (39.22%) | 27 / 59 (45.76%) | 21 / 62 (33.87%) |
| occurrences (all) | 20 | 27 | 21 |
| Loss of appetite | | | |

| | | | |
|---|---|---|---|
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 12 / 51 (23.53%) | 13 / 59 (22.03%) | 14 / 62 (22.58%) |
| occurrences (all) | 12 | 13 | 14 |
| Pyrexia | | | |
| subjects affected / exposed | 7 / 51 (13.73%) | 8 / 59 (13.56%) | 7 / 62 (11.29%) |
| occurrences (all) | 7 | 8 | 7 |
| Gastrointestinal disorders | | | |
| Vomiting | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 3 / 51 (5.88%) | 3 / 59 (5.08%) | 2 / 62 (3.23%) |
| occurrences (all) | 3 | 3 | 2 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 5 / 59 (8.47%) | 5 / 62 (8.06%) |
| occurrences (all) | 1 | 5 | 5 |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 4 / 59 (6.78%) | 12 / 62 (19.35%) |
| occurrences (all) | 1 | 4 | 12 |
| Bronchitis | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | 3 / 59 (5.08%) | 6 / 62 (9.68%) |
| occurrences (all) | 2 | 3 | 6 |
| Upper respiratory tract infection | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | 3 / 59 (5.08%) | 4 / 62 (6.45%) |
| occurrences (all) | 2 | 3 | 4 |
| Viral infection | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 59 (1.69%) | 6 / 62 (9.68%) |
| occurrences (all) | 0 | 1 | 6 |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported