



Clinical trial results:

An open, randomized, phase IIIa study to evaluate the safety and immunogenicity of GlaxoSmithKline Biologicals' 10-valent pneumococcal conjugate vaccine, when administered intramuscularly according to a 2-4-11 months vaccination schedule.

Summary

| | |
|--------------------------|-----------------|
| EudraCT number | 2005-003437-41 |
| Trial protocol | SE DK SK |
| Global end of trial date | 25 January 2007 |

Results information

| | |
|--------------------------------|--|
| Result version number | v2 |
| This version publication date | 20 March 2016 |
| First version publication date | 14 March 2015 |
| Version creation reason | <ul style="list-style-type: none">• Correction of full data setCorrection of errors detected in immunogenicity data |

Trial information

Trial identification

| | |
|-----------------------|--------|
| Sponsor protocol code | 105539 |
|-----------------------|--------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00307034 |
| 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) | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | Yes |
| 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 June 2007 |
| Is this the analysis of the primary completion data? | No |

| | |
|----------------------------------|-----------------|
| Global end of trial reached? | Yes |
| Global end of trial date | 25 January 2007 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To assess the post-dose 2 immune response elicited by GSK Biologicals' 10-valent pneumococcal conjugate vaccine administered according to a 2-4-11 months vaccination schedule with co-administration of DTPa combined vaccine.

Protection of trial subjects:

All subjects were supervised closely for at least 30 minutes following vaccination with appropriate medical treatment readily available. Vaccines 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. Subjects were followed-up from the time the subject consents to participate in the study until she/he is discharged.

Background therapy: -

Evidence for comparator: -

| | |
|---|-----------------|
| Actual start date of recruitment | 05 January 2006 |
| 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 | Norway: 85 |
| Country: Number of subjects enrolled | Slovakia: 75 |
| Country: Number of subjects enrolled | Sweden: 61 |
| Country: Number of subjects enrolled | Denmark: 130 |
| Worldwide total number of subjects | 351 |
| EEA total number of subjects | 351 |

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) | 351 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |

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

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details: -

Pre-assignment period milestones

| | |
|------------------------------|-----|
| Number of subjects started | 351 |
| Number of subjects completed | 351 |

Period 1

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

Arms

| | |
|------------------------------|----------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | 2-dose priming group |

Arm description:

Healthy male or female subjects between, and including 8 to 16 weeks (56-120 days) of age at the time of first vaccination, received a 2-dose primary vaccination course of 10Pn-PD-DiT, vaccine at 2 and 4 months of age, followed by a booster dose of the same vaccine at 11 months of age, each dose being co-administered with one dose of Infanrix hexa™ (DTPa-HBV-IPV/Hib) or Infanrix™ IPV Hib (DTPa-IPV/Hib), according to national recommendations. 10Pn-PD-DiT vaccine was administered intramuscularly into the right anterolateral thigh and DTPa combined vaccine was administered intramuscularly into the left anterolateral thigh.

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | 10-valent Streptococcus pneumoniae conjugate vaccine |
| Investigational medicinal product code | |
| Other name | 10Pn-PD-DiT |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

2 primary doses of 10Pn-PD-DiT vaccine at 2 and 4 months of age, with first vaccine dose at 8-16 weeks of age. A 3rd dose of 10Pn-PD-DiT (i.e. booster dose) was administered at 11 months of age.

| | |
|--|---|
| Investigational medicinal product name | Infanrix hexa™ |
| Investigational medicinal product code | |
| Other name | DTPa-HBV-IPV/Hib, DTPa combined vaccine |
| Pharmaceutical forms | Powder and solvent for suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

2 doses of DTPa combined vaccine administered at 2 and 4 months of age, with first vaccine dose at 8-16 weeks of age. A 3rd dose of DTPa combined vaccine at 11 months of age.

| | |
|--|---|
| Investigational medicinal product name | Infanrix™ IPV Hib |
| Investigational medicinal product code | |
| Other name | DTPa-IPV/Hib, DTPa combined vaccine |
| Pharmaceutical forms | Powder and solvent for suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

2 doses of DTPa combined vaccine administered at 2 and 4 months of age, with first vaccine dose at 8-

16 weeks of age. A 3rd dose of DTPa combined vaccine at 11 months of age.

| | |
|------------------|----------------------|
| Arm title | 3-dose priming group |
|------------------|----------------------|

Arm description:

Healthy male or female subjects between, and including 8 to 16 weeks (56-120 days) of age at the time of first vaccination, received a 3-dose primary vaccination course of 10Pn-PD-DiT, vaccine at 2, 3 and 4 months of age, co-administered with 2 doses of Infanrix hexa™ (DTPa-HBV-IPV/Hib) or Infanrix™ IPV Hib (DTPa-IPV/Hib), according to national recommendations at 2 and 4 months of age, followed by a booster dose of the 10Pn-PD-DiT vaccine at 11 months of age, co-administered with one dose of the DTPa combined vaccine. 10Pn-PD-DiT vaccine was administered intramuscularly into the right anterolateral thigh and DTPa combined vaccine was administered intramuscularly into the left anterolateral thigh.

| | |
|--|--|
| Arm type | Comparator |
| Investigational medicinal product name | 10-valent Streptococcus pneumoniae conjugate vaccine |
| Investigational medicinal product code | |
| Other name | 10Pn-PD-DiT |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

3 primary doses of 10Pn-PD-DiT vaccine and 3 doses of DTPa combined vaccine co-administered at 2, 3 and 4 months of age, with first vaccine dose at 8-16 weeks of age. A 4rd dose of 10Pn-PD-DiT (i.e. booster dose) was co-administered with a 3rd dose of DTPa combined vaccine at 11 months of age.

| | |
|--|---|
| Investigational medicinal product name | Infanrix hexa™ |
| Investigational medicinal product code | |
| Other name | DTPa-HBV-IPV/Hib, DTPa combined vaccine |
| Pharmaceutical forms | Powder and solvent for suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

2 doses of DTPa combined vaccine administered at 2 and 4 months of age, with first vaccine dose at 8-16 weeks of age. A 3rd dose of DTPa combined vaccine at 11 months of age.

| | |
|--|---|
| Investigational medicinal product name | Infanrix™ IPV Hib |
| Investigational medicinal product code | |
| Other name | DTPa-IPV/Hib, DTPa combined vaccine |
| Pharmaceutical forms | Powder and solvent for suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

2 doses of DTPa combined vaccine administered at 2 and 4 months of age, with first vaccine dose at 8-16 weeks of age. A 3rd dose of DTPa combined vaccine at 11 months of age.

| Number of subjects in period 1 | 2-dose priming group | 3-dose priming group |
|--------------------------------|----------------------|----------------------|
| Started | 175 | 176 |
| Completed | 173 | 169 |
| Not completed | 2 | 7 |
| Consent withdrawn by subject | 1 | 2 |
| Adverse event, non-fatal | 1 | 2 |
| Lost to follow-up | - | 3 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|----------------------|
| Reporting group title | 2-dose priming group |
|-----------------------|----------------------|

Reporting group description:

Healthy male or female subjects between, and including 8 to 16 weeks (56-120 days) of age at the time of first vaccination, received a 2-dose primary vaccination course of 10Pn-PD-DiT, vaccine at 2 and 4 months of age, followed by a booster dose of the same vaccine at 11 months of age, each dose being co-administered with one dose of Infanrix hexa™ (DTPa-HBV-IPV/Hib) or Infanrix™ IPV Hib (DTPa-IPV/Hib), according to national recommendations. 10Pn-PD-DiT vaccine was administered intramuscularly into the right anterolateral thigh and DTPa combined vaccine was administered intramuscularly into the left anterolateral thigh.

| | |
|-----------------------|----------------------|
| Reporting group title | 3-dose priming group |
|-----------------------|----------------------|

Reporting group description:

Healthy male or female subjects between, and including 8 to 16 weeks (56-120 days) of age at the time of first vaccination, received a 3-dose primary vaccination course of 10Pn-PD-DiT, vaccine at 2, 3 and 4 months of age, co-administered with 2 doses of Infanrix hexa™ (DTPa-HBV-IPV/Hib) or Infanrix™ IPV Hib (DTPa-IPV/Hib), according to national recommendations at 2 and 4 months of age, followed by a booster dose of the 10Pn-PD-DiT vaccine at 11 months of age, co-administered with one dose of the DTPa combined vaccine. 10Pn-PD-DiT vaccine was administered intramuscularly into the right anterolateral thigh and DTPa combined vaccine was administered intramuscularly into the left anterolateral thigh.

| Reporting group values | 2-dose priming group | 3-dose priming group | Total |
|--|----------------------|----------------------|-------|
| Number of subjects | 175 | 176 | 351 |
| Age categorical | | | |
| 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: weeks | | | |
| arithmetic mean | 12 | 12.1 | |
| standard deviation | ± 1.94 | ± 1.9 | - |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 86 | 82 | 168 |
| Male | 89 | 94 | 183 |

End points

End points reporting groups

| | |
|---|----------------------|
| Reporting group title | 2-dose priming group |
| Reporting group description: Healthy male or female subjects between, and including 8 to 16 weeks (56-120 days) of age at the time of first vaccination, received a 2-dose primary vaccination course of 10Pn-PD-DiT, vaccine at 2 and 4 months of age, followed by a booster dose of the same vaccine at 11 months of age, each dose being co-administered with one dose of Infanrix hexa™ (DTPa-HBV-IPV/Hib) or Infanrix™ IPV Hib (DTPa-IPV/Hib), according to national recommendations. 10Pn-PD-DiT vaccine was administered intramuscularly into the right anterolateral thigh and DTPa combined vaccine was administered intramuscularly into the left anterolateral thigh. | |
| Reporting group title | 3-dose priming group |
| Reporting group description: Healthy male or female subjects between, and including 8 to 16 weeks (56-120 days) of age at the time of first vaccination, received a 3-dose primary vaccination course of 10Pn-PD-DiT, vaccine at 2, 3 and 4 months of age, co-administered with 2 doses of Infanrix hexa™ (DTPa-HBV-IPV/Hib) or Infanrix™ IPV Hib (DTPa-IPV/Hib), according to national recommendations at 2 and 4 months of age, followed by a booster dose of the 10Pn-PD-DiT vaccine at 11 months of age, co-administered with one dose of the DTPa combined vaccine. 10Pn-PD-DiT vaccine was administered intramuscularly into the right anterolateral thigh and DTPa combined vaccine was administered intramuscularly into the left anterolateral thigh. | |

Primary: Number of subjects with anti-pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F antibody concentrations ≥ 0.20 µg/mL

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|--|--|
| 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 ^[1] |
| 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. This outcome concerns results for the Primary Phase of the study. The results presented for the Group 1 correspond to the primary outcome. | |
| End point type | Primary |
| End point timeframe: At Month 3, e.g. one month after the administration of the second dose (in a 2-4-11 months of age vaccination schedule) or one month after the administration of the third dose (in a 2-3-4-11 months of age vaccination schedule) with 10Pn-PD-DiT vaccine. | |

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.

| End point values | 2-dose priming group | 3-dose priming group | | |
|-----------------------------|----------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 153 | 153 | | |
| Units: Subjects | | | | |
| Anti-1 (N= 153, 151) | 149 | 149 | | |
| Anti-4 (N=153, 153) | 150 | 152 | | |
| Anti-5 (N=152, 149) | 146 | 149 | | |
| Anti-6B (N=149, 149) | 83 | 94 | | |

| | | | | |
|-----------------------|-----|-----|--|--|
| Anti-7F (N=153, 152) | 148 | 151 | | |
| Anti-9V (N=152, 153) | 142 | 152 | | |
| Anti-14 (N=152, 152) | 146 | 152 | | |
| Anti-18C (N=152, 153) | 146 | 152 | | |
| Anti-19F (N=152, 152) | 141 | 146 | | |
| Anti-23F (N=153, 152) | 106 | 118 | | |

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 $\geq 0.20 \mu\text{g/mL}$

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|-----------------|--|
| End point title | Number of subjects with Anti-pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F antibody concentrations $\geq 0.20 \mu\text{g/mL}$ |
|-----------------|--|

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 ($\mu\text{g/mL}$). The seropositivity cut-off of the assay was an antibody concentration $\geq 0.05 \mu\text{g/mL}$. This outcome concerns results for the Booster Phase of the study.

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

End point timeframe:

At Month 9, e.g. before the booster dose and at Month 10, e.g. one month after the booster dose of 10Pn-PD-DiT vaccine

| End point values | 2-dose priming group | 3-dose priming group | | |
|-----------------------------------|----------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 156 | 149 | | |
| Units: Subjects | | | | |
| Anti-1 at Month 9 (N= 149, 147) | 77 | 101 | | |
| Anti-1 at Month 10 (N=156, 147) | 155 | 147 | | |
| Anti-4 at Month 9 (N= 152, 149) | 120 | 137 | | |
| Anti-4 at Month 10 (N=155, 147) | 155 | 147 | | |
| Anti-5 at Month 9 (N= 148, 149) | 121 | 133 | | |
| Anti-5 at Month 10 (N=155, 147) | 155 | 147 | | |
| Anti-6B at Month 9 (N= 154, 148) | 101 | 111 | | |
| Anti-6B at Month 10 (N=156, 147) | 138 | 142 | | |
| Anti-7F at Month 9 (N= 151, 149) | 135 | 146 | | |
| Anti-7F at Month 10 (N=156, 147) | 156 | 147 | | |
| Anti-9V at Month 9 (N= 153, 149) | 133 | 142 | | |
| Anti-9V at Month 10 (N=156, 147) | 155 | 147 | | |
| Anti-14 at Month 9 (N= 151, 149) | 140 | 147 | | |
| Anti-14 at Month 10 (N=156, 147) | 155 | 145 | | |
| Anti-18C at Month 9 (N= 154, 149) | 133 | 144 | | |
| Anti-18C at Month 10 (N=156, 147) | 156 | 146 | | |

| | | | | |
|-----------------------------------|-----|-----|--|--|
| Anti-19F at Month 9 (N= 153, 149) | 140 | 143 | | |
| Anti-19F at Month 10 (N=156, 147) | 150 | 144 | | |
| Anti-23F at Month 9 (N= 151, 148) | 108 | 116 | | |
| Anti-23F at Month 10 (N=154, 147) | 148 | 141 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations against pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F

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|-----------------|--|
| End point title | Antibody concentrations against pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F |
|-----------------|--|

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. This outcome concerns results for the Primary and Booster Phases of the study.

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

End point timeframe:

At Month 3, e.g. 1 month after second dose (in a 2-4-11 months of age schedule) or third dose (in a 2-3-4-11 months of age schedule), at Month 9 e.g. before booster dose and at Month 10, e.g. 1 month after booster dose of 10Pn-PD-DiT vaccine.

| End point values | 2-dose priming group | 3-dose priming group | | |
|--|----------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 156 | 153 | | |
| Units: µg/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-1 at Month 3 (N= 153, 151) | 1.03 (0.9 to 1.18) | 1.23 (1.07 to 1.42) | | |
| Anti-1 at Month 9 (N= 149, 147) | 0.21 (0.19 to 0.24) | 0.3 (0.26 to 0.34) | | |
| Anti-1 at Month 10 (N=156, 147) | 1.85 (1.59 to 2.15) | 1.88 (1.62 to 2.17) | | |
| Anti-4 at Month 3 (N= 153, 153) | 1.37 (1.21 to 1.55) | 1.71 (1.47 to 1.99) | | |
| Anti-4 at Month 9 (N= 152, 149) | 0.4 (0.35 to 0.46) | 0.64 (0.56 to 0.73) | | |
| Anti-4 at Month 10 (N=155, 147) | 3.06 (2.68 to 3.49) | 3.47 (3.03 to 3.98) | | |
| Anti-5 at Month 3 (N= 152, 149) | 1.32 (1.14 to 1.52) | 1.85 (1.63 to 2.1) | | |
| Anti-5 at Month 9 (N= 148, 149) | 0.43 (0.37 to 0.5) | 0.59 (0.51 to 0.68) | | |
| Anti-5 at Month 10 (N=155, 147) | 2.65 (2.31 to 3.03) | 3.21 (2.81 to 3.67) | | |
| Anti-6B at Month 3 (N= 149, 149) | 0.19 (0.15 to 0.24) | 0.31 (0.25 to 0.38) | | |

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|-----------------------------------|---------------------|---------------------|--|--|
| Anti-6B at Month 9 (N= 154, 148) | 0.28 (0.23 to 0.35) | 0.44 (0.36 to 0.54) | | |
| Anti-6B at Month 10 (N=156, 147) | 1.12 (0.88 to 1.41) | 1.85 (1.54 to 2.22) | | |
| Anti-7F at Month 3 (N= 153, 152) | 1.28 (1.13 to 1.46) | 2.14 (1.9 to 2.4) | | |
| Anti-7F at Month 9 (N= 151, 149) | 0.55 (0.49 to 0.63) | 0.92 (0.81 to 1.05) | | |
| Anti-7F at Month 10 (N=156, 147) | 2.81 (2.51 to 3.15) | 3.88 (3.45 to 4.37) | | |
| Anti-9V at Month 3 (N= 152, 153) | 0.92 (0.81 to 1.05) | 1.47 (1.29 to 1.68) | | |
| Anti-9V at Month 9 (N= 153, 149) | 0.52 (0.46 to 0.6) | 0.87 (0.77 to 0.99) | | |
| Anti-9V at Month 10 (N=156, 147) | 2.95 (2.59 to 3.37) | 3.97 (3.49 to 4.5) | | |
| Anti-14 at Month 3 (N= 152, 152) | 1.72 (1.45 to 2.05) | 2.57 (2.22 to 2.97) | | |
| Anti-14 at Month 9 (N= 151, 149) | 0.77 (0.64 to 0.93) | 1.53 (1.27 to 1.85) | | |
| Anti-14 at Month 10 (N=156, 147) | 4.19 (3.62 to 4.85) | 5.47 (4.68 to 6.4) | | |
| Anti-18C at Month 3 (N= 152, 153) | 1.26 (1.06 to 1.51) | 3.42 (2.87 to 4.07) | | |
| Anti-18C at Month 9 (N= 154, 149) | 0.59 (0.5 to 0.69) | 1.14 (0.96 to 1.35) | | |
| Anti-18C at Month 10 (N=156, 147) | 6.24 (5.43 to 7.18) | 7.2 (6.08 to 8.52) | | |
| Anti-19F at Month 3 (N= 152, 152) | 2.43 (1.97 to 2.98) | 4.43 (3.6 to 5.45) | | |
| Anti-19F at Month 9 (N= 153, 149) | 1.04 (0.87 to 1.25) | 1.7 (1.41 to 2.04) | | |
| Anti-19F at Month 10 (N=156, 147) | 5.58 (4.65 to 6.69) | 6.95 (5.92 to 8.17) | | |
| Anti-23F at Month 3 (N= 153, 152) | 0.38 (0.3 to 0.47) | 0.52 (0.42 to 0.63) | | |
| Anti-23F at Month 9 (N= 151, 148) | 0.32 (0.26 to 0.4) | 0.44 (0.36 to 0.54) | | |
| Anti-23F at Month 10 (N=154, 147) | 2.41 (1.98 to 2.94) | 2.78 (2.31 to 3.35) | | |

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

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

End point description:

Seropositivity status defined as Opsonophagocytic activity against pneumococcal serotypes ≥ 8 . This outcome concerns results for the Primary and Booster Phases of the study.

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

End point timeframe:

At Month 3, e.g. 1 month after second dose (in a 2-4-11 months of age schedule) or third dose (in a 2-3-4-11 months of age schedule), at Month 9 e.g. before booster dose and at Month 10, e.g. 1 month

| End point values | 2-dose priming group | 3-dose priming group | | |
|--|---------------------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 136 | 135 | | |
| Units: Titers | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Opsono-1 at Month 3 (N= 130, 132) | 21.9 (16.4 to 29.1) | 26.5 (19.8 to 35.4) | | |
| Opsono-1 at Month 9 (N= 136, 134) | 5.1 (4.5 to 5.8) | 6.7 (5.4 to 8.3) | | |
| Opsono-1 at Month 10 (N=131, 126) | 109.9 (76.1 to 158.7) | 100.6 (68.9 to 146.9) | | |
| Opsono-4 at Month 3 (N= 134, 132) | 462.6 (410.4 to 521.4) | 758.9 (647.8 to 888.9) | | |
| Opsono-4 at Month 9 (N= 104, 114) | 13.8 (9.7 to 19.6) | 18.6 (12.7 to 27.2) | | |
| Opsono-4 at Month 10 (N=125, 101) | 634.6 (496.3 to 811.3) | 1204 (990.7 to 1463.2) | | |
| Opsono-5 at Month 3 (N= 132, 130) | 48.3 (37.7 to 61.8) | 68.4 (54 to 86.5) | | |
| Opsono-5 at Month 9 (N= 133, 135) | 9.9 (8.1 to 12) | 10.7 (8.6 to 13.4) | | |
| Opsono-5 at Month 10 (N=133, 121) | 102.1 (75.8 to 137.6) | 157.2 (123.1 to 200.7) | | |
| Opsono-6B at Month 3 (N= 125, 126) | 157.8 (104.7 to 237.8) | 379.6 (272.4 to 529.1) | | |
| Opsono-6B at Month 9 (N= 121, 124) | 56.1 (34.9 to 90.4) | 62.9 (40.2 to 98.5) | | |
| Opsono-6B at Month 10 (N=132, 103) | 220.3 (146.9 to 330.3) | 468.5 (311.6 to 704.3) | | |
| Opsono-7F at Month 3 (N= 127, 131) | 844.8 (591.4 to 1206.7) | 2176.5 (1759.2 to 2692.7) | | |
| Opsono-7F at Month 9 (N= 113, 126) | 148.5 (89.5 to 246.4) | 380.6 (253 to 572.6) | | |
| Opsono-7F at Month 10 (N=128, 109) | 1843.4 (1494.2 to 2274.1) | 3290.6 (2709.1 to 3996.8) | | |
| Opsono-9V at Month 3 (N= 134, 132) | 875.1 (732 to 1046.1) | 1343.4 (1130.8 to 1596) | | |
| Opsono-9V at Month 9 (N= 120, 134) | 266.8 (205.1 to 347.1) | 322.2 (256.4 to 405.1) | | |
| Opsono-9V at Month 10 (N=129, 109) | 1068.1 (874.7 to 1304.2) | 1706.9 (1438.5 to 2025.3) | | |
| Opsono-14 at Month 3 (N= 132, 131) | 692.6 (559.1 to 858) | 1125.3 (946.2 to 1338.3) | | |
| Opsono-14 at Month 9 (N= 102, 123) | 52.1 (32.4 to 84) | 157.3 (108.5 to 228.1) | | |
| Opsono-14 at Month 10 (N=107, 101) | 835.5 (672.1 to 1038.5) | 1280.7 (1054.5 to 1555.5) | | |
| Opsono-18C at Month 3 (N= 134, 131) | 56.2 (42.9 to 73.7) | 218.6 (176.1 to 271.4) | | |

| | | | | |
|-------------------------------------|--------------------------|--------------------------|--|--|
| Opsono-18C at Month 9 (N= 122, 126) | 8.3 (6.5 to 10.7) | 16.9 (12.5 to 22.8) | | |
| Opsono-18C at Month 10 (N=136, 130) | 330 (259.1 to 420.3) | 490.8 (395.3 to 609.4) | | |
| Opsono-19F at Month 3 (N= 131, 128) | 101 (74.9 to 136) | 356.7 (263.2 to 483.4) | | |
| Opsono-19F at Month 9 (N= 130, 134) | 16.5 (12.9 to 21.1) | 31.6 (24.5 to 40.8) | | |
| Opsono-19F at Month 10 (N=131, 129) | 251.3 (193.4 to 326.6) | 734.7 (568.3 to 949.8) | | |
| Opsono-23F at Month 3 (N= 131, 129) | 489.7 (342.6 to 700) | 1233.7 (991.7 to 1534.7) | | |
| Opsono-23F at Month 9 (N= 112, 133) | 190.7 (115.2 to 315.6) | 150.7 (95.9 to 236.8) | | |
| Opsono-23F at Month 10 (N=134, 121) | 1047.3 (748.1 to 1466.3) | 1528.9 (1171.2 to 1996) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of antibodies against protein D (ANTI-PD)

| | |
|-----------------|--|
| End point title | Concentrations of antibodies against protein D (ANTI-PD) |
|-----------------|--|

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. This outcome concerns results for the Primary and Booster Phases of the study.

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

End point timeframe:

At Month 3, e.g. 1 month after second dose (in a 2-4-11 months of age schedule) or third dose (in a 2-3-4-11 months of age schedule), at Month 9 e.g. before booster dose and at Month 10, e.g. 1 month after booster dose of 10Pn-PD-DiT vaccine.

| End point values | 2-dose priming group | 3-dose priming group | | |
|--|---------------------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 154 | 148 | | |
| Units: EL.U/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-PD at Month 3 (N=149, 148) | 861.8 (740.4 to 1003.1) | 1223.3 (1066.5 to 1403.2) | | |
| Anti-PD at Month 9 (N= 151, 148) | 349.7 (294.2 to 415.7) | 499.8 (425.3 to 587.2) | | |
| Anti-PD at Month 10 (N= 154, 146) | 1629.8 (1346.4 to 1972.8) | 2113 (1808.9 to 2468.2) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of antibodies against diphtheria (Anti-D) and tetanus (Anti-T).

| | |
|-----------------|--|
| End point title | Concentrations of antibodies against diphtheria (Anti-D) and tetanus (Anti-T). |
|-----------------|--|

End point description:

Concentrations of antibodies are presented as geometric mean concentrations expressed as International units per milliliter (IU/mL). Seroprotection status defined as Anti-diphtheria and anti-tetanus toxoid antibody concentrations ≥ 0.1 IU/mL This outcome concerns results for the Primary and Booster Phases of the study.

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

End point timeframe:

At Month 3, e.g. one month after the administration of the second dose, at Month 9, e.g. before the booster dose and at Month 10, e.g. one month after the booster dose of DTPa combined vaccine

| End point values | 2-dose priming group | 3-dose priming group | | |
|--|------------------------|-------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 156 | 151 | | |
| Units: IU/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-D at Month 3 (N=154, 151) | 1.791 (1.503 to 2.133) | 3.123 (2.621 to 3.723) | | |
| Anti-D at Month 9 (N= 154, 148) | 0.326 (0.275 to 0.386) | 0.725 (0.622 to 0.846) | | |
| Anti-D at Month 10 (N= 156, 148) | 5.423 (4.815 to 6.108) | 8.262 (7.339 to 9.301) | | |
| Anti-T at Month 3 (N=154, 151) | 2.504 (2.17 to 2.89) | 4.602 (4.062 to 5.213) | | |
| Anti-T at Month 9 (N= 153, 149) | 0.565 (0.487 to 0.656) | 1.191 (1.055 to 1.344) | | |
| Anti-T at Month 10 (N= 156, 148) | 7.678 (6.997 to 8.425) | 9.597 (8.749 to 10.526) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of antibodies against polyribosyl ribitol phosphate (Anti-PRP)

| | |
|--|---|
| End point title | Concentrations of antibodies against polyribosyl ribitol phosphate (Anti-PRP) |
| End point description: Concentrations of antibodies are presented as geometric mean concentrations expressed as micrograms per milliliter (µg/mL). Seroprotection status defined as anti-PRP antibody concentrations ≥ 0.15 µg/mL and ≥ 1.0 µg/mL. This outcome concerns results for the Primary and Booster Phases of the study. | |
| End point type | Secondary |
| End point timeframe: At Month 3, e.g. one month after the administration of the second dose, at Month 9, e.g. before the booster dose and at Month 10, e.g. one month after the booster dose of DTPa combined vaccine | |

| End point values | 2-dose priming group | 3-dose priming group | | |
|--|---------------------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 155 | 148 | | |
| Units: µg/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-PRP at Month 3 (N=146, 147) | 1.179 (0.893 to 1.556) | 2.186 (1.648 to 2.9) | | |
| Anti-PRP at Month 9 (N= 150, 148) | 0.431 (0.349 to 0.532) | 0.777 (0.613 to 0.984) | | |
| Anti-PRP at Month 10 (N= 155, 147) | 16.943 (13.485 to 21.287) | 21.654 (17.263 to 27.161) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of antibodies against pertussis toxoid (Anti-PT), against filamentous haemagglutinin (Anti-FHA) and pertactin (Anti-PRN)

| | |
|--|---|
| End point title | Concentrations of antibodies against pertussis toxoid (Anti-PT), against filamentous haemagglutinin (Anti-FHA) and pertactin (Anti-PRN) |
| End point description: Concentrations of antibodies are presented as geometric mean concentrations expressed as enzyme-linked immunosorbent assay (ELISA) unit per milliliter (EL.U/mL). Seropositivity status defined as anti-PT, anti-FHA and anti-PRN antibody concentrations ≥ 5 EL.U/mL. This outcome concerns results for the Primary and Booster Phases of the study. | |
| End point type | Secondary |
| End point timeframe: At Month 3, e.g. one month after the administration of the second dose, at Month 9, e.g. before the booster dose and at Month 10, e.g. one month after the booster dose of DTPa combined vaccine | |

| End point values | 2-dose priming group | 3-dose priming group | | |
|--|------------------------|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 150 | 147 | | |
| Units: EL.U/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-PT at Month 3 (N=145, 144) | 36.1 (32.9 to 39.6) | 33.8 (30.2 to 37.9) | | |
| Anti-PT at Month 9 (N= 144, 145) | 9.8 (8.7 to 11.1) | 10.2 (8.9 to 11.7) | | |
| Anti-PT at Month 10 (N= 149, 145) | 78.2 (70.5 to 86.8) | 65.5 (58.7 to 73.1) | | |
| Anti-FHA at Month 3 (N=145, 144) | 166.7 (150.1 to 185.2) | 142.2 (125.6 to 161.1) | | |
| Anti-FHA at Month 9 (N= 144, 145) | 46.6 (41.3 to 52.6) | 46.9 (41.1 to 53.6) | | |
| Anti-FHA at Month 10 (N= 149, 144) | 360.3 (323.7 to 401) | 276.6 (249.4 to 306.7) | | |
| Anti-PRN at Month 3 (N=145, 144) | 83.9 (69.6 to 101.1) | 89 (74.1 to 106.8) | | |
| Anti-PRN at Month 9 (N= 144, 145) | 13.7 (11.2 to 16.6) | 18 (14.8 to 21.8) | | |
| Anti-PRN at Month 10 (N= 150, 147) | 275.5 (235.9 to 321.7) | 209.3 (181.8 to 241) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of antibodies against hepatitis B surface antigen (Anti-HBs) (subset of subjects who received DTPa-HBV-IPV/Hib as co-administered vaccine)

| | |
|-----------------|---|
| End point title | Concentrations of antibodies against hepatitis B surface antigen (Anti-HBs) (subset of subjects who received DTPa-HBV-IPV/Hib as co-administered vaccine) |
|-----------------|---|

End point description:

Concentrations of antibodies are presented as geometric mean concentrations expressed as milli International units per milliliter (IU/mL). Seroprotection status defined as Anti-HBs antibody concentrations ≥ 10 mIU/mL.. This outcome concerns results for the Primary and Booster Phases of the study.

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

End point timeframe:

At Month 3, e.g. one month after the administration of the second dose, at Month 9, e.g. before the booster dose and at Month 10, e.g. one month after the booster dose of DTPa combined vaccine

| End point values | 2-dose priming group | 3-dose priming group | | |
|--|---------------------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 40 | 46 | | |
| Units: mIU/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-HBs at Month 3 (N=37, 38) | 293.7 (195.9 to 440.5) | 478.6 (294.8 to 776.9) | | |
| Anti-HBs at Month 9 (N= 40, 46) | 84.3 (55.4 to 128.2) | 156.6 (106.4 to 230.4) | | |
| Anti-HBs at Month 10 (N= 27, 28) | 1892.3 (1012.2 to 3537.6) | 2922.4 (2010.4 to 4248.1) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Titers of antibodies against polio type 1, 2 and 3 (Anti-polio 1, 2 and 3) (subset of subjects who received DTPa-HBV-IPV/Hib as co-administered vaccine)

| | |
|-----------------|--|
| End point title | Titers of antibodies against polio type 1, 2 and 3 (Anti-polio 1, 2 and 3) (subset of subjects who received DTPa-HBV-IPV/Hib as co-administered vaccine) |
|-----------------|--|

End point description:

Titers of antibodies are presented as geometric mean titers. Seroprotection status is defined as anti-Polio types 1, 2 and 3 antibody titers ≥ 8 . This outcome concerns results for the Primary and Booster Phases of the study.

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

End point timeframe:

At Month 3, e.g. one month after the administration of the second dose, at Month 9, e.g. before the booster dose and at Month 10, e.g. one month after the booster dose of DTPa combined vaccine

| End point values | 2-dose priming group | 3-dose priming group | | |
|--|--------------------------|-------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 50 | 59 | | |
| Units: Titer | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-Polio 1 at Month 3 (N=47, 57) | 88.5 (56.3 to 139.1) | 99.1 (63.4 to 154.8) | | |
| Anti-Polio 1 at Month 9 (N=45,39) | 24.6 (15.6 to 38.8) | 14.4 (8.9 to 23.1) | | |
| Anti-Polio 1 at Month 10 (N=20,15) | 1006.4 (541.8 to 1869.4) | 645 (399.4 to 1041.7) | | |
| Anti-Polio 2 at Month 3 (N=47,59) | 57.7 (36.8 to 90.6) | 40.5 (25 to 65.6) | | |
| Anti-Polio 2 at Month 9 (N=44,40) | 14.9 (10.7 to 20.9) | 10.9 (7.2 to 16.4) | | |
| Anti-Polio 2 at Month 10 (N=17,14) | 522.4 (235.7 to 1157.7) | 512.2 (186.4 to 1407.7) | | |

| | | | | |
|-----------------------------------|---------------------------|-------------------------|--|--|
| Anti-Polio 3 at Month 3 (N=50,57) | 165.6 (109.3 to 250.8) | 161 (98.7 to 262.8) | | |
| Anti-Polio 3 at Month 9 (N=44,38) | 15.1 (9.8 to 23.2) | 14.7 (9 to 24.1) | | |
| Anti-Polio 3 at Month 10 (N=5,11) | 1910.8 (257.4 to 14185.3) | 961.4 (388.3 to 2380.6) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with booster vaccine response to Anti-PT, Anti-FHA and Anti-PRN antibody

| | |
|-----------------|---|
| End point title | Number of subjects with booster vaccine response to Anti-PT, Anti-FHA and Anti-PRN antibody |
|-----------------|---|

End point description:

Booster vaccine response to PT, FHA and PRN, defined as the appearance of antibodies in subjects who were seronegative (Pre-booster status S-) (i.e., with antibody concentrations < 5 EL.U/mL) just before booster dose, and at least two-fold increase of pre-vaccination antibody concentrations in those who were seropositive (Pre-booster status S+) (i.e., with antibody concentrations ≥ 5 EL.U/mL) just before booster dose

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

End point timeframe:

At Month 10, e.g. one month after the administration of the booster dose

| End point values | 2-dose priming group | 3-dose priming group | | |
|--|----------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 137 | 142 | | |
| Units: Subjects | | | | |
| Anti-PT-Pre-booster status S-(N=20,23) | 20 | 23 | | |
| Anti-PT-Pre-booster status S+(N=117,117) | 115 | 114 | | |
| Anti-PT-Pre-booster status Total(N=137,140) | 135 | 137 | | |
| Anti-FHA-Pre-booster status S-(N=0,1) | 0 | 1 | | |
| Anti-FHA-Pre-booster status S+(N=137,138) | 132 | 129 | | |
| Anti-FHA-Pre-booster status Total(N=137,139) | 132 | 130 | | |
| Anti-PRN-Pre-booster status S-(N=35,21) | 35 | 21 | | |
| Anti-PRN-Pre-booster status S+(N=102,121) | 101 | 119 | | |
| Anti-PRN-Pre-booster status Total(N=137,142) | 136 | 140 | | |

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).

Across doses= across the 2 doses of the 10Pn-PD-DiT vaccine in the 2-dose priming group and across the 3 doses of the 10Pn-PD-DiT vaccine in the 3-dose priming group.

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

End point timeframe:

During the 4-day (Day 0-3) period following the primary vaccination (across doses) and during the 4-day (Day 0-3) period following the booster vaccination (post Bst) with the 10PN-PD-DT vaccine.

| End point values | 2-dose priming group | 3-dose priming group | | |
|--|----------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 175 | 176 | | |
| Units: Subjects | | | | |
| Any Pain, across doses (N=175;176) | 92 | 110 | | |
| Grade 3 Pain, across doses (N=175;176) | 14 | 12 | | |
| Any Redness, across doses (N=175;176) | 137 | 135 | | |
| Grade 3 Redness, across doses (N=175;176) | 4 | 6 | | |
| Any Swelling, across doses (N=175;176) | 111 | 105 | | |
| Grade 3 Swelling, across doses (N=175;176) | 20 | 16 | | |
| Any Pain, post Bst (N=174,169) | 103 | 93 | | |
| Grade 3 Pain, post Bst (N=174,169) | 7 | 5 | | |
| Any Redness, post Bst (N=174,169) | 118 | 115 | | |
| Grade 3 Redness, post Bst (N=174,169) | 20 | 20 | | |
| Any Swelling, post Bst (N=174,169) | 97 | 99 | | |
| Grade 3 Swelling, post Bst (N=174,169) | 19 | 15 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number/percentage of subjects with solicited general symptoms

| | |
|-----------------|---|
| End point title | Number/percentage of subjects with 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 [\geq] 38.0 degrees Celsius [$^{\circ}$ 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 activity. Grade 3 Irr./Fuss. = Crying that could not be comforted/prevented normal activity. Grade 3 Loss of appetite = Subject did not eat at all. Grade 3 Fever = Rectal temperature higher than (>) 40.0°C. Across doses= across the 2 doses of the 10Pn-PD-DiT vaccine in the 2-dose priming group and across the 3 doses of the 10Pn-PD-DiT vaccine in the 3-dose priming group.

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

End point timeframe:

During the 4-day (Day 0-3) period following the primary vaccination (across doses) and during the 4-day (Day 0-3) period following the booster vaccination (post Bst) with the 10PN-PD-DT vaccine.

| End point values | 2-dose priming group | 3-dose priming group | | |
|---|----------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 175 | 176 | | |
| Units: Subjects | | | | |
| Any Drowsiness, across doses (N=175;176) | 130 | 130 | | |
| Grade 3 Drowsiness, across doses (N=175,176) | 9 | 4 | | |
| Related Drowsiness, across doses (N=175,176) | 123 | 124 | | |
| Any Fever, across doses (N=175,176) | 108 | 116 | | |
| Grade 3 Fever, across doses (N=175,176) | 0 | 0 | | |
| Related Fever, across doses (N=175,176) | 106 | 108 | | |
| Any Irr./Fuss., across doses (N=175,176) | 149 | 158 | | |
| Grade 3 Irr./Fuss., across doses (N=175,176) | 18 | 28 | | |
| Related Irr./Fuss., across doses (N=175,176) | 142 | 147 | | |
| Any Loss Appet., across doses (N=175,176) | 81 | 88 | | |
| Grade 3 Loss Appet., across doses (N=175,176) | 5 | 1 | | |
| Related Loss Appet., across doses (N=175,176) | 75 | 81 | | |
| Any Drowsiness, post Bst (N=174,169) | 97 | 79 | | |
| Grade 3 Drowsiness, post Bst (N=174,169) | 6 | 2 | | |
| Related Drowsiness, post Bst (N=174,169) | 83 | 71 | | |
| Any Fever, post Bst (N=174,169) | 96 | 78 | | |
| Grade 3 Fever, post Bst (N=174,169) | 1 | 0 | | |
| Related Fever, post Bst (N=174,169) | 84 | 67 | | |
| Any Irr./Fuss., post Bst (N=174,169) | 113 | 104 | | |
| Grade 3 Irr./Fuss., post Bst (N=174,169) | 6 | 2 | | |
| Related Irr./Fuss., post Bst (N=174,169) | 99 | 89 | | |
| Any Loss Appet., post Bst (N=174,169) | 61 | 56 | | |
| Grade 3 Loss Appet., post Bst (N=174,169) | 3 | 0 | | |

| | | | | |
|--|----|----|--|--|
| Related Loss Appet., post Bst (N=174,169) | 53 | 43 | | |
|--|----|----|--|--|

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 primary vaccination, across doses

| End point values | 2-dose priming group | 3-dose priming group | | |
|-----------------------------|----------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 175 | 176 | | |
| Units: Subjects | | | | |
| Any AE | 78 | 114 | | |

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 booster vaccination.

| End point values | 2-dose priming group | 3-dose priming group | | |
|-----------------------------|----------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 174 | 171 | | |
| Units: Subjects | | | | |
| Any AE | 63 | 72 | | |

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 primary vaccination period | |

| End point values | 2-dose priming group | 3-dose priming group | | |
|-----------------------------|----------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 175 | 176 | | |
| Units: Subjects | | | | |
| Any SAE | 5 | 7 | | |

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 booster vaccination period. | |

| End point values | 2-dose priming group | 3-dose priming group | | |
|-----------------------------|----------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 174 | 171 | | |
| Units: Subjects | | | | |
| Any SAE | 2 | 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 days post-primary vaccination (across doses) and post-booster dose.
Unsolicited AEs: during 31 days post-primary vaccination (across doses) and post-booster dose. SAEs: during both primary and booster vaccination periods

Adverse event reporting additional description:

Analysis of AEs and SAEs was done on subjects with at least 1 primary vaccination dose. Analysis of solicited symptoms was done on subjects with at least 1 primary dose and with results available. 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 | 10.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|----------------------|
| Reporting group title | 2-dose priming Group |
|-----------------------|----------------------|

Reporting group description:

Group 1

| | |
|-----------------------|----------------------|
| Reporting group title | 3-dose priming Group |
|-----------------------|----------------------|

Reporting group description:

Group 2

| Serious adverse events | 2-dose priming Group | 3-dose priming Group | |
|---|---|----------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 5 / 175 (2.86%) | 7 / 176 (3.98%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Nervous system disorders | | | |
| Febrile convulsion | Additional description: Reported during Booster phase | | |
| subjects affected / exposed ^[1] | 1 / 174 (0.57%) | 0 / 171 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Dyspepsia | Additional description: Reported during Primary phase | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 176 (0.57%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Asthma | Additional description: Reported during Primary phase | | |

| | | | |
|---|---|-----------------|--|
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 176 (0.57%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Dermatitis allergic | Additional description: Reported during Primary phase | | |
| subjects affected / exposed | 1 / 175 (0.57%) | 0 / 176 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Respiratory syncytial virus infection | Additional description: Reported during Primary phase | | |
| subjects affected / exposed | 1 / 175 (0.57%) | 1 / 176 (0.57%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchopneumonia | Additional description: Reported during Primary phase | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 176 (0.57%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis | Additional description: Reported during Primary phase | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 176 (0.57%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis viral | Additional description: Reported during Primary phase | | |
| subjects affected / exposed | 1 / 175 (0.57%) | 0 / 176 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lower respiratory tract infection | Additional description: Reported during Primary phase | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 176 (0.57%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Salmonellosis | Additional description: Reported during Primary phase | | |
| subjects affected / exposed | 1 / 175 (0.57%) | 0 / 176 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tracheitis | Additional description: Reported during Primary phase | | |

| | | | |
|---|---|-----------------|--|
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 176 (0.57%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract infection-Primary phase | Additional description: Reported during Primary phase | | |
| subjects affected / exposed | 0 / 175 (0.00%) | 1 / 176 (0.57%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Viral infection | Additional description: Reported during Primary phase | | |
| subjects affected / exposed | 1 / 175 (0.57%) | 0 / 176 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Otitis media | Additional description: Reported during Booster phase | | |
| subjects affected / exposed ^[2] | 0 / 174 (0.00%) | 1 / 171 (0.58%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia | Additional description: Reported during Booster phase | | |
| subjects affected / exposed ^[3] | 1 / 174 (0.57%) | 0 / 171 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract infection-Booster phase | Additional description: Reported during Booster phase | | |
| subjects affected / exposed ^[4] | 1 / 174 (0.57%) | 0 / 171 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: Analysis of serious adverse events during the booster phase was done on subjects with at least 1 primary dose and with results available during this phase.

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: Analysis of serious adverse events during the booster phase was done on subjects with at least 1 primary dose and with results available during this phase.

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: Analysis of serious adverse events during the booster phase was done on subjects with at least 1 primary dose and with results available during this phase.

[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: Analysis of serious adverse events during the booster phase was done on subjects with at least 1 primary dose and with results available during this phase.

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

| Non-serious adverse events | 2-dose priming Group | 3-dose priming Group | |
|---|----------------------|----------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 149 / 175 (85.14%) | 158 / 176 (89.77%) | |
| General disorders and administration site conditions | | | |
| Pain-primary phase | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 92 / 175 (52.57%) | 110 / 176 (62.50%) | |
| occurrences (all) | 92 | 110 | |
| Redness-primary phase | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 137 / 175 (78.29%) | 135 / 176 (76.70%) | |
| occurrences (all) | 137 | 135 | |
| Swelling-primary phase | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 111 / 175 (63.43%) | 105 / 176 (59.66%) | |
| occurrences (all) | 111 | 105 | |
| Pain-booster phase | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed ^[5] | 103 / 174 (59.20%) | 93 / 169 (55.03%) | |
| occurrences (all) | 103 | 93 | |
| Redness-booster phase | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed ^[6] | 118 / 174 (67.82%) | 115 / 169 (68.05%) | |
| occurrences (all) | 118 | 115 | |
| Swelling-booster phase | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed ^[7] | 97 / 174 (55.75%) | 99 / 169 (58.58%) | |
| occurrences (all) | 97 | 99 | |
| Drowsiness-primary phase | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 130 / 175 (74.29%) | 130 / 176 (73.86%) | |
| occurrences (all) | 130 | 130 | |
| Fever (rectally, ≥38°C)-primary phase | | | |
| alternative assessment type: Systematic | | | |

| | | | |
|--|--------------------|--------------------|--|
| subjects affected / exposed | 108 / 175 (61.71%) | 116 / 176 (65.91%) | |
| occurrences (all) | 108 | 116 | |
| Irritability-primary phase | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 149 / 175 (85.14%) | 158 / 176 (89.77%) | |
| occurrences (all) | 149 | 158 | |
| Loss of appetite-primary phase | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 81 / 175 (46.29%) | 88 / 176 (50.00%) | |
| occurrences (all) | 81 | 88 | |
| Drowsiness-booster phase | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed ^[8] | 97 / 174 (55.75%) | 79 / 169 (46.75%) | |
| occurrences (all) | 97 | 79 | |
| Fever (rectally, $\geq 38^{\circ}\text{C}$)-booster phase | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed ^[9] | 96 / 174 (55.17%) | 78 / 169 (46.15%) | |
| occurrences (all) | 96 | 78 | |
| Irritability-booster phase | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed ^[10] | 113 / 174 (64.94%) | 104 / 169 (61.54%) | |
| occurrences (all) | 113 | 104 | |
| Loss of appetite-booster phase | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed ^[11] | 61 / 174 (35.06%) | 56 / 169 (33.14%) | |
| occurrences (all) | 61 | 56 | |
| Pyrexia-primary phase | | | |
| subjects affected / exposed | 12 / 175 (6.86%) | 12 / 176 (6.82%) | |
| occurrences (all) | 12 | 12 | |
| Pyrexia-booster phase | | | |
| subjects affected / exposed ^[12] | 8 / 174 (4.60%) | 10 / 171 (5.85%) | |
| occurrences (all) | 8 | 10 | |
| Gastrointestinal disorders | | | |

| | | | |
|--|-------------------------|-------------------------|--|
| Diarrhoea subjects affected / exposed occurrences (all) | 11 / 175 (6.29%) 11 | 8 / 176 (4.55%) 8 | |
| Vomiting subjects affected / exposed occurrences (all) | 4 / 175 (2.29%) 4 | 10 / 176 (5.68%) 10 | |
| Respiratory, thoracic and mediastinal disorders Cough-primary phase subjects affected / exposed occurrences (all) | 9 / 175 (5.14%) 9 | 9 / 176 (5.11%) 9 | |
| Cough-booster phase subjects affected / exposed ^[13] occurrences (all) | 6 / 174 (3.45%) 6 | 11 / 171 (6.43%) 11 | |
| Infections and infestations Nasopharyngitis-primary phase subjects affected / exposed occurrences (all) | 26 / 175 (14.86%) 26 | 46 / 176 (26.14%) 46 | |
| Nasopharyngitis-booster phase subjects affected / exposed ^[14] occurrences (all) | 16 / 174 (9.20%) 16 | 20 / 171 (11.70%) 20 | |
| Otitis media subjects affected / exposed ^[15] occurrences (all) | 9 / 174 (5.17%) 9 | 7 / 171 (4.09%) 7 | |

Notes:

[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: Analysis of adverse events during the booster phase was done on subjects with at least 1 primary dose and with results available during this phase.

[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: Analysis of adverse events during the booster phase was done on subjects with at least 1 primary dose and with results available during this phase.

[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: Analysis of adverse events during the booster phase was done on subjects with at least 1 primary dose and with results available during this phase.

[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: Analysis of adverse events during the booster phase was done on subjects with at least 1 primary dose and with results available during this phase.

[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: Analysis of adverse events during the booster phase was done on subjects with at least 1 primary dose and with results available during this phase.

[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: Analysis of adverse events during the booster phase was done on subjects with at least 1 primary dose and with results available during this phase.

[11] - 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: Analysis of adverse events during the booster phase was done on subjects with at least 1 primary dose and with results available during this phase.

[12] - 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: Analysis of adverse events during the booster phase was done on subjects with at least 1 primary dose and with results available during this phase.

[13] - 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: Analysis of adverse events during the booster phase was done on subjects with at least 1 primary dose and with results available during this phase.

[14] - 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: Analysis of adverse events during the booster phase was done on subjects with at least 1 primary dose and with results available during this phase.

[15] - 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: Analysis of adverse events during the booster phase was done on subjects with at least 1 primary dose and with results available during this phase.

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