



Clinical trial results:

A phase III, randomized, open, controlled study to assess the immunogenicity, safety and reactogenicity of GlaxoSmithKline (GSK) Biologicals' 10-valent pneumococcal conjugate vaccine as a 3-dose primary immunization course at 6, 10 and 14 weeks of age in Sub-Saharan Africa, co-administered with GSK Biologicals' DTPw-HBV/Hib and OPV vaccines.

Due to a system error, the data reported in v1 is not correct and has been removed from public view.

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2011-004650-25 |
| Trial protocol | Outside EU/EEA |
| Global end of trial date | 10 December 2009 |

Results information

| | |
|--------------------------------|---|
| Result version number | v2 |
| This version publication date | 07 April 2016 |
| First version publication date | 05 July 2015 |
| Version creation reason | <ul style="list-style-type: none">• Correction of full data set Data correction due to a system error in EudraCT – Results: categories issue. A few data (typos) were corrected in some endpoints. |

Trial information

Trial identification

| | |
|-----------------------|--------|
| Sponsor protocol code | 110521 |
|-----------------------|--------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00678301 |
| 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, 44 2089904466, GSKClinicalSupportHD@gsk.com |
| Scientific contact | Clinical Trials Call Center, GlaxoSmithKline Biologicals, 44 2089904466, 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? | No |

| | |
|--|-----|
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | Yes |
|--|-----|

Notes:

Results analysis stage

| | |
|--|-----------------|
| Analysis stage | Final |
| Date of interim/final analysis | 13 October 2010 |
| Is this the analysis of the primary completion data? | No |

| | |
|----------------------------------|------------------|
| Global end of trial reached? | Yes |
| Global end of trial date | 10 December 2009 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To evaluate the immunogenicity of GSK Biologicals' 10-valent pneumococcal conjugate vaccine in Sub-Saharan Africa, one month post dose 3.

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 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 consented to participate in the study through consent by his/her parents/guardians until she/he was discharged.

Background therapy: -

Evidence for comparator: -

| | |
|---|--------------|
| Actual start date of recruitment | 18 June 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 | Nigeria: 127 |
| Country: Number of subjects enrolled | Mali: 238 |
| Worldwide total number of subjects | 365 |
| EEA total number of subjects | 0 |

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) | 365 |

| | |
|---------------------------|---|
| 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:

At screening, the following steps occurred: check for inclusion/exclusion criteria, contraindications/precautions, medical and vaccination history of the subjects and signing or thumb-printing informed consent forms.

Pre-assignment period milestones

| | |
|------------------------------|-----|
| Number of subjects started | 365 |
| Number of subjects completed | 357 |

Pre-assignment subject non-completion reasons

| | |
|----------------------------|---------------------------|
| Reason: Number of subjects | Subject not vaccinated: 8 |
|----------------------------|---------------------------|

Period 1

| | |
|------------------------------|---|
| Period 1 title | Entire Study period (Months 0-3) (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|-----------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | 10Pn-PD-DiT/EPI Group |

Arm description:

Subjects in this group received 3 doses of 10Pn-PD-DiT vaccine, GSK Biologicals' 10-valent pneumococcal conjugate 1024850A vaccine (later marketed as Synflorix) according to a 3-dose schedule at 6-10-14 weeks of age co-administered with 3 doses of Expanded Program on Immunization (EPI) vaccines Zilbrix™ Hib (or DTPw-HBV/Hib) and Polio Sabin™ (or OPV) according to the same schedule. The 10Pn-PD-DiT and DTPw-HBV/Hib vaccines were administered by intramuscular injection, in the right and left thigh respectively. The OPV vaccine was administered orally.

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | 10-valent streptococcus pneumoniae conjugate vaccine |
| Investigational medicinal product code | 10Pn-PD-DiT |
| Other name | 10Pn, 10Pn-PD-DiT, GSK1024850A, Synflorix |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

The 10Pn-PD-DiT vaccine was administered by intramuscular injection, in the right thigh, according to a 3-dose schedule at 6-10-14 weeks of age.

| | |
|--|-----------------|
| Investigational medicinal product name | Polio Sabin |
| Investigational medicinal product code | |
| Other name | OPV |
| Pharmaceutical forms | Oral suspension |
| Routes of administration | Oral use |

Dosage and administration details:

The OPV vaccine was administered orally, according to a 3-dose schedule at 6-10-14 weeks of age.

| | |
|--|--------------|
| Investigational medicinal product name | Zilbrix Hib |
| Investigational medicinal product code | |
| Other name | DTPw-HBV/Hib |

| | |
|--------------------------|--|
| Pharmaceutical forms | Powder and solution for solution for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

The DTPw-HBV/Hib vaccine was administered by intramuscular injection, in the left thigh, according to a 3-dose schedule at 6-10-14 weeks of age.

| | |
|------------------|-----------|
| Arm title | EPI Group |
|------------------|-----------|

Arm description:

Subjects in this group received 3 doses of Expanded Program on Immunization (EPI) vaccines Zilbrix™ Hib (or DTPw-HBV/Hib) and Polio Sabin™ (or OPV) according to a 3-dose schedule at 6-10-14 weeks of age. The DTPw-HBV/Hib vaccine was administered by intramuscular injection, in the left thigh. The OPV vaccine was administered orally.

| | |
|--|-------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | Polio Sabin |
| Investigational medicinal product code | |
| Other name | OPV |
| Pharmaceutical forms | Oral suspension |
| Routes of administration | Oral use |

Dosage and administration details:

The OPV vaccine was administered orally, according to a 3-dose schedule at 6-10-14 weeks of age.

| | |
|--|--|
| Investigational medicinal product name | Zilbrix Hib |
| Investigational medicinal product code | |
| Other name | DTPw-HBV/Hib |
| Pharmaceutical forms | Powder and solution for solution for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

The DTPw-HBV/Hib vaccine was administered by intramuscular injection, in the left thigh, according to a 3-dose schedule at 6-10-14 weeks of age.

| Number of subjects in period 1^[1] | 10Pn-PD-DiT/EPI Group | EPI Group |
|---|-----------------------|-----------|
| Started | 239 | 118 |
| Completed | 231 | 116 |
| Not completed | 8 | 2 |
| Consent withdrawn by subject | 4 | - |
| Adverse event, non-fatal | 1 | - |
| Lost to follow-up | 3 | 1 |
| Non-compliance with study procedures | - | 1 |

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: 365 subjects were enrolled but 8 subjects didn't received vaccination.

Baseline characteristics

Reporting groups

| | |
|---|-----------------------|
| Reporting group title | 10Pn-PD-DiT/EPI Group |
| Reporting group description: | |
| Subjects in this group received 3 doses of 10Pn-PD-DiT vaccine, GSK Biologicals' 10-valent pneumococcal conjugate 1024850A vaccine (later marketed as Synflorix) according to a 3-dose schedule at 6-10-14 weeks of age co-administered with 3 doses of Expanded Program on Immunization (EPI) vaccines Zilbrix™ Hib (or DTPw-HBV/Hib) and Polio Sabin™ (or OPV) according to the same schedule. The 10Pn-PD-DiT and DTPw-HBV/Hib vaccines were administered by intramuscular injection, in the right and left thigh respectively. The OPV vaccine was administered orally. | |
| Reporting group title | EPI Group |
| Reporting group description: | |
| Subjects in this group received 3 doses of Expanded Program on Immunization (EPI) vaccines Zilbrix™ Hib (or DTPw-HBV/Hib) and Polio Sabin™ (or OPV) according to a 3-dose schedule at 6-10-14 weeks of age. The DTPw-HBV/Hib vaccine was administered by intramuscular injection, in the left thigh. The OPV vaccine was administered orally. | |

| Reporting group values | 10Pn-PD-DiT/EPI Group | EPI Group | Total |
|--|-----------------------|-----------|-------|
| Number of subjects | 239 | 118 | 357 |
| 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 | 7.1 | 7 | |
| standard deviation | ± 1.15 | ± 1.18 | - |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 119 | 62 | 181 |
| Male | 120 | 56 | 176 |

End points

End points reporting groups

| | |
|---|-----------------------|
| Reporting group title | 10Pn-PD-DiT/EPI Group |
| Reporting group description: | |
| Subjects in this group received 3 doses of 10Pn-PD-DiT vaccine, GSK Biologicals' 10-valent pneumococcal conjugate 1024850A vaccine (later marketed as Synflorix) according to a 3-dose schedule at 6-10-14 weeks of age co-administered with 3 doses of Expanded Program on Immunization (EPI) vaccines Zilbrix™ Hib (or DTPw-HBV/Hib) and Polio Sabin™ (or OPV) according to the same schedule. The 10Pn-PD-DiT and DTPw-HBV/Hib vaccines were administered by intramuscular injection, in the right and left thigh respectively. The OPV vaccine was administered orally. | |
| Reporting group title | EPI Group |
| Reporting group description: | |
| Subjects in this group received 3 doses of Expanded Program on Immunization (EPI) vaccines Zilbrix™ Hib (or DTPw-HBV/Hib) and Polio Sabin™ (or OPV) according to a 3-dose schedule at 6-10-14 weeks of age. The DTPw-HBV/Hib vaccine was administered by intramuscular injection, in the left thigh. The OPV vaccine was administered orally. | |

Primary: Concentrations of antibodies against vaccine pneumococcal serotypes

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|--|--|
| End point title | Concentrations of antibodies against vaccine pneumococcal serotypes ^[1] |
| End point description: | |
| Pneumococcal serotypes assessed were vaccine pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F. Seropositivity cut-off for the assay was an anti-pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F antibody (Anti-1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F) concentrations \geq 0.05 microgram per milliliter ($\mu\text{g/mL}$). | |
| End point type | Primary |
| End point timeframe: | |
| At Month 3, one month after the administration of the third dose of 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 | 10Pn-PD-DiT/EPI Group | EPI Group | | |
|--|-----------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 217 | 112 | | |
| Units: $\mu\text{g/mL}$ | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-1 [N=217;108] | 2.69 (2.42 to 2.99) | 0.03 (0.03 to 0.03) | | |
| Anti-4 [N=217;112] | 3.44 (3.06 to 3.87) | 0.03 (0.03 to 0.03) | | |
| Anti-5 [N=217;109] | 4.17 (3.75 to 4.63) | 0.03 (0.03 to 0.04) | | |
| Anti-6B [N=217;112] | 0.95 (0.76 to 1.2) | 0.03 (0.03 to 0.03) | | |
| Anti-7F [N=217;110] | 3.33 (2.99 to 3.71) | 0.03 (0.03 to 0.04) | | |
| Anti-9V [N=217;112] | 2.39 (2.06 to 2.76) | 0.04 (0.03 to 0.05) | | |

| | | | | |
|----------------------|----------------------|---------------------|--|--|
| Anti-14 [N=217;112] | 3.8 (3.24 to 4.46) | 0.14 (0.11 to 0.17) | | |
| Anti-18C [N=217;112] | 10.01 (8.49 to 11.8) | 0.03 (0.03 to 0.04) | | |
| Anti-19F [N=217;111] | 7.65 (6.55 to 8.93) | 0.08 (0.07 to 0.1) | | |
| Anti-23F [N=217;112] | 1.1 (0.91 to 1.33) | 0.03 (0.03 to 0.04) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Antibody concentrations against protein D (anti-PD antibodies)

| | |
|-----------------|--|
| End point title | Antibody concentrations against protein D (anti-PD |
|-----------------|--|

End point description:

Anti-PD antibody concentrations were tabulated, expressed in enzyme-linked immunorbent assay (ELISA) units per millilitre (EL.U/mL). Seropositivity cut-off for the assay was an anti-PD antibody concentrations ≥ 100 EL.U/mL.

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

End point timeframe:

At Month 3, one month after the administration of the third dose of 10Pn-PD-DiT vaccine

Notes:

[2] - 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 | 10Pn-PD-DiT/EPI Group | EPI Group | | |
|--|---------------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 217 | 112 | | |
| Units: EL.U/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-PD | 3791.8 (3448.4 to 4169.3) | 85.4 (71.8 to 101.5) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of antibodies against cross-reactive pneumococcal serotypes 6A and 19A (Anti-6A and -19A)

| | |
|-----------------|--|
| End point title | Concentrations of antibodies against cross-reactive pneumococcal serotypes 6A and 19A (Anti-6A and -19A) |
|-----------------|--|

End point description:

Seropositivity status was defined as anti-pneumococcal cross-reactive serotypes 6A/19A antibody concentrations (Anti-6A/19A) ≥ 0.05 microgram per milliliter ($\mu\text{g/mL}$).

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

End point timeframe:

At Month 3, one month after the administration of the third dose of 10Pn-PD-DiT vaccine

| End point values | 10Pn-PD-DiT/EPI Group | EPI Group | | |
|--|-----------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 217 | 108 | | |
| Units: µg/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-6A | 0.09 (0.08 to 0.11) | 0.04 (0.04 to 0.05) | | |
| Anti-19A | 0.15 (0.13 to 0.18) | 0.06 (0.05 to 0.07) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Titers for opsonophagocytic activity (OPA) against vaccine pneumococcal serotypes

| | |
|-----------------|---|
| End point title | Titers for opsonophagocytic activity (OPA) against vaccine pneumococcal serotypes |
|-----------------|---|

End point description:

Pneumococcal serotypes assessed were vaccine pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F. Seropositivity status was defined as an opsonophagocytic activity against vaccine pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F (OPA-1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F) ≥ 8 .

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

End point timeframe:

At Month 3, one month after the administration of the third dose of 10Pn-PD-DiT vaccine

| End point values | 10Pn-PD-DiT/EPI Group | EPI Group | | |
|--|-----------------------|------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 105 | 56 | | |
| Units: Titers | | | | |
| geometric mean (confidence interval 95%) | | | | |
| OPA-1 [N=105;56] | 83 (61.7 to 111.7) | 5 (3.8 to 6.4) | | |
| OPA-4 [N=105;55] | 892.5 (759.4 to 1049) | 4.6 (3.9 to 5.5) | | |
| OPA-5 [N=105;56] | 82.7 (65.4 to 104.4) | 4.5 (3.8 to 5.2) | | |
| OPA-6B [N=103;54] | 538.6 (346 to 838.3) | 5.7 (4.1 to 7.9) | | |

| | | | | |
|--------------------|--------------------------|-------------------|--|--|
| OPA-7F [N=105;49] | 2733 (2188.3 to 3413.3) | 31.5 (15.5 to 64) | | |
| OPA-9V [N=105;54] | 1023.7 (784.8 to 1335.2) | 8.4 (5.8 to 12.4) | | |
| OPA-14 [N=104;53] | 1079.2 (776 to 1500.9) | 8.9 (5.7 to 14.1) | | |
| OPA-18C [N=105;56] | 617.6 (495.3 to 770) | 4.4 (3.8 to 5.2) | | |
| OPA-19F [N=105;56] | 358.3 (269.9 to 475.5) | 4.6 (3.8 to 5.7) | | |
| OPA-23F [N=104;53] | 881.8 (615 to 1264.4) | 6.6 (4.2 to 10.3) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Titers for opsonophagocytic activity (OPA) against cross-reactive pneumococcal serotypes

| | |
|-----------------|--|
| End point title | Titers for opsonophagocytic activity (OPA) against cross-reactive pneumococcal serotypes |
|-----------------|--|

End point description:

Pneumococcal serotypes assessed were cross-reactive pneumococcal serotypes 6A and 19A. Seropositivity status was defined as an opsonophagocytic activity against cross-reactive pneumococcal serotypes 6A and 19A (OPA-6A and 19A) ≥ 8 .

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

End point timeframe:

At Month 3, one month after the administration of the third dose of 10Pn-PD-DiT vaccine

| End point values | 10Pn-PD-DiT/EPI Group | EPI Group | | |
|--|-----------------------|------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 105 | 56 | | |
| Units: Titres | | | | |
| geometric mean (confidence interval 95%) | | | | |
| OPA-6A [N=101;56] | 14.1 (9.4 to 21.2) | 6.1 (4.4 to 8.7) | | |
| OPA-19A [N=105;56] | 11 (8.3 to 14.6) | 4.3 (4 to 4.6) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seropositive for antibodies against vaccine pneumococcal serotypes

| | |
|-----------------|---|
| End point title | Number of subjects seropositive for antibodies against vaccine pneumococcal serotypes |
|-----------------|---|

End point description:

Pneumococcal serotypes assessed were vaccine pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F. Seropositivity cut-off for the assay was an anti-pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F antibody (Anti-1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F) concentrations \geq 0.05 microgram per milliliter ($\mu\text{g/mL}$).

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

End point timeframe:

At Month 3, one month after the administration of the third dose of 10Pn-PD-DiT vaccine

| End point values | 10Pn-PD-DiT/EPI Group | EPI Group | | |
|-----------------------------|-----------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 217 | 108 | | |
| Units: Subjects | | | | |
| Anti-1 [N=217;108] | 217 | 14 | | |
| Anti-4 [N=217;112] | 217 | 12 | | |
| Anti-5 [N=217;109] | 217 | 18 | | |
| Anti-6B [N=217;112] | 196 | 15 | | |
| Anti-7F [N=217;110] | 217 | 19 | | |
| Anti-9V [N=217;112] | 213 | 31 | | |
| Anti-14 [N=217;112] | 217 | 91 | | |
| Anti-18C [N=217;112] | 216 | 23 | | |
| Anti-19F [N=217;111] | 217 | 73 | | |
| Anti-23F [N=217;112] | 207 | 23 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seroprotected as regards antibodies against vaccine pneumococcal serotypes

| | |
|-----------------|---|
| End point title | Number of subjects seroprotected as regards antibodies against vaccine pneumococcal serotypes |
|-----------------|---|

End point description:

Pneumococcal serotypes assessed were vaccine pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F. Seroprotection cut-off for the assay was an anti-pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F antibody (Anti-1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F) concentrations \geq 0.2 microgram per milliliter ($\mu\text{g/mL}$).

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

End point timeframe:

At Month 3, one month after the administration of the third dose of 10Pn-PD-DiT vaccine

| End point values | 10Pn-PD-DiT/EPI Group | EPI Group | | |
|-----------------------------|-----------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 217 | 112 | | |
| Units: Subjects | | | | |
| Anti-1 [N=217;108] | 217 | 2 | | |
| Anti-4 [N=217;112] | 217 | 3 | | |
| Anti-5 [N=217;109] | 217 | 4 | | |
| Anti-6B [N=217;112] | 178 | 2 | | |
| Anti-7F [N=217;110] | 216 | 2 | | |
| Anti-9V [N=217;112] | 211 | 11 | | |
| Anti-14 [N=217;112] | 215 | 40 | | |
| Anti-18C [N=217;112] | 216 | 4 | | |
| Anti-19F [N=217;111] | 214 | 25 | | |
| Anti-23F [N=217;112] | 190 | 3 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seropositive as regards antibodies against cross-reactive pneumococcal serotypes 6A and 19A (Anti-6A and -19A).

| | |
|-----------------|--|
| End point title | Number of subjects seropositive as regards antibodies against cross-reactive pneumococcal serotypes 6A and 19A (Anti-6A and -19A). |
|-----------------|--|

End point description:

Serotypes assessed were cross-reactive pneumococcal serotypes 6A and 19A. Seropositivity status was defined as anti-pneumococcal cross-reactive serotypes 6A/19A antibody concentrations (Anti-6A/19A) ≥ 0.05 microgram per milliliter ($\mu\text{g/mL}$).

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

End point timeframe:

At Month 3, one month after the administration of the third dose of 10Pn-PD-DiT vaccine

| End point values | 10Pn-PD-DiT/EPI Group | EPI Group | | |
|-----------------------------|-----------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 217 | 108 | | |
| Units: Subjects | | | | |
| Anti-6A | 152 | 36 | | |
| Anti-19A | 176 | 49 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seroprotected as regards antibodies against cross-

reactive pneumococcal serotypes 6A and 19A (Anti-6A and -19A).

| | |
|-----------------|---|
| End point title | Number of subjects seroprotected as regards antibodies against cross-reactive pneumococcal serotypes 6A and 19A (Anti-6A and -19A). |
|-----------------|---|

End point description:

Serotypes assessed were cross-reactive pneumococcal serotypes 6A and 19A. Seroprotection cut-off for the assay was an anti-6A/19A antibody concentrations ≥ 0.2 microgram per milliliter ($\mu\text{g/mL}$).

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

End point timeframe:

At Month 3, one month after the administration of the third dose of 10Pn-PD-DiT vaccine

| End point values | 10Pn-PD-DiT/EPI Group | EPI Group | | |
|-----------------------------|-----------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 217 | 108 | | |
| Units: Subjects | | | | |
| Anti-6A | 56 | 8 | | |
| Anti-19A | 95 | 15 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seropositive as regards antibodies against protein D (Anti-PD antibodies)

| | |
|-----------------|--|
| End point title | Number of subjects seropositive as regards antibodies against protein D (Anti-PD antibodies) |
|-----------------|--|

End point description:

Seropositivity cut-off for the assay was an anti-PD antibody concentrations ≥ 100 EL.U/mL.

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

End point timeframe:

At Month 3, one month after the administration of the third dose of 10Pn-PD-DiT vaccine

| End point values | 10Pn-PD-DiT/EPI Group | EPI Group | | |
|-----------------------------|-----------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 217 | 112 | | |
| Units: Subjects | | | | |
| Anti-PD | 217 | 34 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seropositive as regards opsonophagocytic activity against vaccine pneumococcal serotypes

| | |
|-----------------|---|
| End point title | Number of subjects seropositive as regards opsonophagocytic activity against vaccine pneumococcal serotypes |
|-----------------|---|

End point description:

Pneumococcal serotypes assessed were vaccine pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F. Seropositivity status was defined as an opsonophagocytic activity against vaccine pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F (OPA-1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F) ≥ 8 .

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

End point timeframe:

At Month 3, one month after the administration of the third dose of 10Pn-PD-DiT vaccine

| End point values | 10Pn-PD-DiT/EPI Group | EPI Group | | |
|-----------------------------|-----------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 105 | 56 | | |
| Units: Subjects | | | | |
| OPA-1 [N=105;56] | 92 | 3 | | |
| OPA-4 [N=105;55] | 105 | 3 | | |
| OPA-5 [N=105;56] | 100 | 2 | | |
| OPA-6B [N=103;54] | 88 | 5 | | |
| OPA-7F [N=105;49] | 105 | 21 | | |
| OPA-9V [N=105;54] | 103 | 13 | | |
| OPA-14 [N=104;53] | 100 | 13 | | |
| OPA-18C [N=105;56] | 103 | 2 | | |
| OPA-19F [N=105;56] | 101 | 2 | | |
| OPA-23F [N=104;53] | 97 | 5 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seropositive as regards opsonophagocytic activity against cross-reactive pneumococcal serotypes

| | |
|-----------------|--|
| End point title | Number of subjects seropositive as regards opsonophagocytic activity against cross-reactive pneumococcal serotypes |
|-----------------|--|

End point description:

Pneumococcal serotypes assessed were cross-reactive pneumococcal serotypes 6A and 19A. Seropositivity status was defined as an opsonophagocytic activity against cross-reactive pneumococcal serotypes 6A and 19A (OPA-6A and 19A) ≥ 8 .

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

End point timeframe:

At Month 3, one month after the administration of the third dose of 10Pn-PD-DiT vaccine

| End point values | 10Pn-PD-DiT/EPI Group | EPI Group | | |
|-----------------------------|-----------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 105 | 56 | | |
| Units: Subjects | | | | |
| OPA-6A [N=101;56] | 31 | 6 | | |
| OPA-19A [N=105;56] | 39 | 3 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-Bordetella pertussis (anti-BPT) antibody concentrations

| | |
|---|--|
| End point title | Anti-Bordetella pertussis (anti-BPT) antibody concentrations |
| End point description: | |
| Anti-BPT antibody concentrations were measured, and tabulated in enzyme-linked immunosorbent assay (ELISA) unit per millilitre (EL.U/mL). Seropositivity cut-off for the assay was defined as an anti-BPT antibody concentrations ≥ 15 EL.U/mL | |
| End point type | Secondary |
| End point timeframe: | |
| At Month 3, one month after the administration of the third dose of DTPw-HBV/Hib vaccine | |

| End point values | 10Pn-PD-DiT/EPI Group | EPI Group | | |
|--|-----------------------|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 110 | 111 | | |
| Units: EL.U/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-BPT | 111.9 (102 to 122.7) | 124.9 (111.7 to 139.7) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seropositive as regards anti-Bordetella pertussis (anti-BPT) antibodies

| | |
|---|--|
| End point title | Number of subjects seropositive as regards anti-Bordetella pertussis (anti-BPT) antibodies |
| End point description: | |
| Seropositivity cut-off for the assay was defined as an anti-BPT antibody concentration ≥ 15 enzyme-linked immunosorbent assay (ELISA) unit per millilitre (EL.U/mL). | |

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| At Month 3, one month after the administration of the third dose of DTPw-HBV/Hib vaccine | |

| End point values | 10Pn-PD-DiT/EPI Group | EPI Group | | |
|-----------------------------|-----------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 110 | 111 | | |
| Units: Subjects | | | | |
| Anti-BPT | 110 | 111 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-diphtheria (Anti-D) and anti-tetanus toxoids (Anti-TT) antibody concentrations

| | |
|--|---|
| End point title | Anti-diphtheria (Anti-D) and anti-tetanus toxoids (Anti-TT) antibody concentrations |
| End point description: | |
| The seroprotection cut-off for the endpoint was an anti-diphtheria toxoid or anti-tetanus toxoid antibody concentrations ≥ 0.1 international unit per milliliter (IU/mL). | |
| End point type | Secondary |
| End point timeframe: | |
| At Month 3, one month after the administration of the third dose of DTPw-HBV/Hib vaccine | |

| End point values | 10Pn-PD-DiT/EPI Group | EPI Group | | |
|--|------------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 110 | 112 | | |
| Units: IU/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-D | 4.103 (3.527 to 4.773) | 3.13 (2.731 to 3.588) | | |
| Anti-T | 6.484 (5.511 to 7.628) | 4.588 (3.88 to 5.426) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seroprotected as regards anti-diphtheria (Anti D) and anti-tetanus toxoids (Anti TT) antibodies

| | |
|---|--|
| End point title | Number of subjects seroprotected as regards anti-diphtheria (Anti D) and anti-tetanus toxoids (Anti TT) antibodies |
| End point description: A seroprotected subject as regards anti-D/-TT antibodies was defined as a subject with an Anti-D/-TT antibody concentration ≥ 0.1 international unit per milliliter (IU/mL). | |
| End point type | Secondary |
| End point timeframe: At Month 3, one month after the administration of the third dose of DTPw-HBV/Hib vaccine | |

| End point values | 10Pn-PD-DiT/EPI Group | EPI Group | | |
|-----------------------------|-----------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 110 | 112 | | |
| Units: Subjects | | | | |
| Anti-D | 110 | 112 | | |
| Anti-T | 110 | 112 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-polyribosyl-ribitol-phosphate (Anti-PRP) antibody concentrations

| | |
|---|---|
| End point title | Anti-polyribosyl-ribitol-phosphate (Anti-PRP) antibody concentrations |
| End point description: Anti-PRP antibody concentrations were measured and tabulated in microgram per millilitre ($\mu\text{g/mL}$). Cut-off for the assay was $\geq 0.15 \mu\text{g/mL}$. | |
| End point type | Secondary |
| End point timeframe: At Month 3, one month after the administration of the third dose of DTPw-HBV/Hib vaccine | |

| End point values | 10Pn-PD-DiT/EPI Group | EPI Group | | |
|--|---------------------------|--------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 110 | 112 | | |
| Units: $\mu\text{g/mL}$ | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-PRP | 18.461 (14.256 to 23.907) | 10.137 (7.515 to 13.673) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seroprotected as regards anti-polyribosyl-ribitol phosphate (anti-PRP) antibodies, for the ≥ 0.15 $\mu\text{g/mL}$ cut-off

| | |
|-----------------|--|
| End point title | Number of subjects seroprotected as regards anti-polyribosyl-ribitol phosphate (anti-PRP) antibodies, for the ≥ 0.15 $\mu\text{g/mL}$ cut-off |
|-----------------|--|

End point description:

Anti-PRP antibody concentrations were measured and tabulated in microgram per millilitre ($\mu\text{g/mL}$). The seroprotection cut-off applied for this endpoint was ≥ 0.15 $\mu\text{g/mL}$.

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

End point timeframe:

At Month 3, one month after the administration of the third dose of DTPw-HBV/Hib vaccine

| End point values | 10Pn-PD-DiT/EPI Group | EPI Group | | |
|-----------------------------|-----------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 110 | 112 | | |
| Units: Subjects | | | | |
| Anti-PRP | 110 | 111 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seroprotected as regards anti-polyribosyl-ribitol phosphate (anti-PRP) antibodies, for the ≥ 1 $\mu\text{g/mL}$ cut-off

| | |
|-----------------|---|
| End point title | Number of subjects seroprotected as regards anti-polyribosyl-ribitol phosphate (anti-PRP) antibodies, for the ≥ 1 $\mu\text{g/mL}$ cut-off |
|-----------------|---|

End point description:

Anti-PRP antibody concentrations were measured and tabulated in microgram per millilitre ($\mu\text{g/mL}$). The seroprotection cut-off applied for this endpoint was ≥ 1 $\mu\text{g/mL}$.

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

End point timeframe:

At Month 3, one month after the administration of the third dose of DTPw-HBV/Hib vaccine

| End point values | 10Pn-PD-DiT/EPI Group | EPI Group | | |
|-----------------------------|-----------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 110 | 112 | | |
| Units: Subjects | | | | |
| Anti-PRP | 107 | 102 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-hepatitis B surface antigen (HBs) antibody concentrations

| | |
|-----------------|--|
| End point title | Anti-hepatitis B surface antigen (HBs) antibody concentrations |
|-----------------|--|

End point description:

The seroprotection cut-off for the endpoint was an anti-HBs antibody concentration ≥ 10 milli-international units per milliliter (mIU/mL). Please note that a decrease in the specificity of the anti-HBs Enzyme-Linked ImmunoSorbent Assay (ELISA) assay had been observed in some studies for low levels of antibody (10-100 mIU/mL). The results presented are updated results following partial or complete retesting/reanalysis.

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

End point timeframe:

At Month 3, one month after the administration of the third dose of DTPw-HBV/Hib vaccine

| End point values | 10Pn-PD-DiT/EPI Group | EPI Group | | |
|--|-------------------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 91 | 96 | | |
| Units: mIU/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-HBs | 1835.1 (1384 to 2433.2) | 1485.5 (1198.7 to 1840.9) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seroprotected as regards anti-Hepatitis B surface antigen (HBs) antibodies.

| | |
|-----------------|--|
| End point title | Number of subjects seroprotected as regards anti-Hepatitis B surface antigen (HBs) antibodies. |
|-----------------|--|

End point description:

The seroprotection cut-off values considered for this endpoint were an anti-HBs antibody concentration ≥ 10 and 100 milli-international units per milliliter (mIU/mL). This follows from that a decrease in the specificity of the anti-HBs Enzyme-Linked ImmunoSorbent Assay (ELISA) assay had been observed in some studies for low levels of antibody (10-100 mIU/mL). The results presented are updated results following partial or complete retesting/reanalysis.

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

End point timeframe:

At Month 3, one month after the administration of the third dose of DTPw-HBV/Hib vaccine

| End point values | 10Pn-PD-DiT/EPI Group | EPI Group | | |
|-----------------------------|-----------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 91 | 96 | | |
| Units: Subjects | | | | |
| Anti-HBs \geq 10 mIU/mL | 89 | 96 | | |
| Anti-HBs \geq 100 mIU/mL | 89 | 94 | | |

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Solicited local symptoms assessed include pain, redness and swelling. Grade 3 pain was defined as crying when limb was moved/spontaneously painful. Grade 3 swelling/redness was defined as swelling/redness larger than ($>$) 30 millimeters (mm). "Any" is defined as incidence of the specified symptom regardless of intensity.

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

End point timeframe:

Within the 4-day (Days 0 to 3) follow-up periods after each vaccination, across doses and across vaccines

| End point values | 10Pn-PD-DiT/EPI Group | EPI Group | | |
|-----------------------------|-----------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 239 | 118 | | |
| Units: Subjects | | | | |
| Any Pain | 234 | 112 | | |
| Grade 3 Pain | 8 | 3 | | |
| Any Redness | 57 | 30 | | |
| Grade 3 Redness | 0 | 0 | | |
| Any Swelling | 173 | 83 | | |
| Grade 3 Swelling | 22 | 11 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any and any Grade 3 and related solicited

general symptoms

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

End point description:

Solicited general symptoms assessed include drowsiness, fever (defined as rectal temperature $\geq 38.0^{\circ}\text{C}$), irritability, and loss of appetite. "Any" is defined as incidence of the specified symptom regardless of intensity or relationship to study vaccination. Grade 3 drowsiness was defined as drowsiness which prevented normal everyday activities. Grade 3 fever was defined as fever (rectal temperature) above ($>$) 40.0°C . Grade 3 irritability was defined as crying that could not be comforted/preventing normal activity. Grade 3 loss of appetite was defined as the subject not eating at all.

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

End point timeframe:

Within the 4-day (Days 0 to 3) follow-up periods after each vaccination, across doses and across vaccines

| End point values | 10Pn-PD-DiT/EPI Group | EPI Group | | |
|-----------------------------|-----------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 239 | 118 | | |
| Units: Subjects | | | | |
| Any Drowsiness | 24 | 12 | | |
| Grade 3 Drowsiness | 0 | 0 | | |
| Any Fever (Rectally) | 207 | 105 | | |
| Grade 3 Fever (Rectally) | 1 | 0 | | |
| Any Irritability | 192 | 88 | | |
| Grade 3 Irritability | 6 | 2 | | |
| Any Loss of appetite | 37 | 15 | | |
| Grade 3 Loss of appetite | 1 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with fever (temperature measured rectally $> 39.0^{\circ}\text{C}$)

| | |
|-----------------|---|
| End point title | Number of subjects with fever (temperature measured rectally $> 39.0^{\circ}\text{C}$) |
|-----------------|---|

End point description:

The level of fever (fever being as rectal temperature $\geq 38.0^{\circ}\text{C}$) assessed for this endpoint was $> 39.0^{\circ}\text{C}$.

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

End point timeframe:

Within the 4-day (Days 0 to 3) follow-up periods after each vaccination, across doses and across vaccines

| End point values | 10Pn-PD-DiT/EPI Group | EPI Group | | |
|-----------------------------|-----------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 239 | 118 | | |
| Units: Subjects | | | | |
| Fever >39.0°C | 40 | 13 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with unsolicited adverse events (AEs)

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

End point description:

An AE is 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. "Any" was defined an incidence of an unsolicited AE regardless of intensity or relationship to study vaccination.

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

End point timeframe:

Within the 31-day (Days 0-30) follow-up periods post vaccination, across doses and across vaccines

| End point values | 10Pn-PD-DiT/EPI Group | EPI Group | | |
|-----------------------------|-----------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 239 | 118 | | |
| Units: Subjects | | | | |
| Any AEs | 176 | 92 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with serious adverse events (SAEs)

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

End point description:

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

End point timeframe:

Throughout the entire study period, from Month 0 to Month 3

| End point values | 10Pn-PD-DiT/EPI Group | EPI Group | | |
|-----------------------------|-----------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 239 | 118 | | |
| Units: Subjects | | | | |
| Any SAEs | 5 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited symptoms and unsolicited AEs: During the 4-day (Days 0-3) and 31-day (Days 0-30) post vaccination follow-up periods, respectively, across doses and across vaccines. SAEs: throughout the entire study period, from Month 0 to Month 3.

Adverse event reporting additional description:

The occurrence of reported AEs (all/related) was not available and is encoded as equal to the number of subjects affected.

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

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 12.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-----------|
| Reporting group title | EPI Group |
|-----------------------|-----------|

Reporting group description:

Subjects in this group received 3 doses of Expanded Program on Immunization (EPI) vaccines Zilbrix™ Hib (or DTPw-HBV/Hib) and Polio Sabin™ (or OPV) according to a 3-dose schedule at 6-10-14 weeks of age. The DTPw-HBV/Hib vaccine was administered by intramuscular injection, in the left thigh. The OPV vaccine was administered orally.

| | |
|-----------------------|-----------------------|
| Reporting group title | 10Pn-PD-DiT/EPI Group |
|-----------------------|-----------------------|

Reporting group description:

Subjects in this group received 3 doses of 10Pn-PD-DiT vaccine, GSK Biologicals' 10-valent pneumococcal conjugate 1024850A vaccine (later marketed as Synflorix) according to a 3-dose schedule at 6-10-14 weeks of age co-administered with 3 doses of Expanded Program on Immunization (EPI) vaccines Zilbrix™ Hib (or DTPw-HBV/Hib) and Polio Sabin™ (or OPV) according to the same schedule. The 10Pn-PD-DiT and DTPw-HBV/Hib vaccines were administered by intramuscular injection, in the right and left thigh respectively. The OPV vaccine was administered orally.

| Serious adverse events | EPI Group | 10Pn-PD-DiT/EPI Group | |
|---|-----------------|-----------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 118 (0.00%) | 5 / 239 (2.09%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | | | |
| Vascular disorders | | | |
| Bronchopneumonia | | | |
| subjects affected / exposed | 0 / 118 (0.00%) | 4 / 239 (1.67%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haematoma | | | |
| subjects affected / exposed | 0 / 118 (0.00%) | 1 / 239 (0.42%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|-----------------|-----------------|--|
| Nervous system disorders | | | |
| Febrile convulsion | | | |
| subjects affected / exposed | 0 / 118 (0.00%) | 1 / 239 (0.42%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Malaria | | | |
| subjects affected / exposed | 0 / 118 (0.00%) | 1 / 239 (0.42%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | EPI Group | 10Pn-PD-DiT/EPI Group | |
|---|--------------------|-----------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 112 / 118 (94.92%) | 234 / 239 (97.91%) | |
| General disorders and administration site conditions | | | |
| Pain | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 112 / 118 (94.92%) | 234 / 239 (97.91%) | |
| occurrences (all) | 112 | 234 | |
| Redness | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 30 / 118 (25.42%) | 57 / 239 (23.85%) | |
| occurrences (all) | 30 | 57 | |
| Swelling | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 83 / 118 (70.34%) | 173 / 239 (72.38%) | |
| occurrences (all) | 83 | 173 | |
| Drowsiness | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 12 / 118 (10.17%) | 24 / 239 (10.04%) | |
| occurrences (all) | 12 | 24 | |
| Fever (rectal temperature $\geq 38.5^{\circ}\text{C}$) | | | |
| alternative assessment type: | | | |

| | | | |
|---|--------------------|--------------------|--|
| Systematic | | | |
| subjects affected / exposed | 105 / 118 (88.98%) | 207 / 239 (86.61%) | |
| occurrences (all) | 105 | 207 | |
| Irritability | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 88 / 118 (74.58%) | 192 / 239 (80.33%) | |
| occurrences (all) | 88 | 192 | |
| Loss of appetite | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 15 / 118 (12.71%) | 37 / 239 (15.48%) | |
| occurrences (all) | 15 | 37 | |
| Injection site erosion | | | |
| subjects affected / exposed | 6 / 118 (5.08%) | 1 / 239 (0.42%) | |
| occurrences (all) | 6 | 1 | |
| Injection site induration | | | |
| subjects affected / exposed | 20 / 118 (16.95%) | 22 / 239 (9.21%) | |
| occurrences (all) | 20 | 22 | |
| Eye disorders | | | |
| Conjunctivitis | | | |
| subjects affected / exposed | 16 / 118 (13.56%) | 35 / 239 (14.64%) | |
| occurrences (all) | 16 | 35 | |
| Gastrointestinal disorders | | | |
| Abdominal distension | | | |
| subjects affected / exposed | 22 / 118 (18.64%) | 43 / 239 (17.99%) | |
| occurrences (all) | 22 | 43 | |
| Gastrointestinal disorder | | | |
| subjects affected / exposed | 15 / 118 (12.71%) | 25 / 239 (10.46%) | |
| occurrences (all) | 15 | 25 | |
| Stomatitis | | | |
| subjects affected / exposed | 4 / 118 (3.39%) | 13 / 239 (5.44%) | |
| occurrences (all) | 4 | 13 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Allergic bronchitis | | | |
| subjects affected / exposed | 46 / 118 (38.98%) | 83 / 239 (34.73%) | |
| occurrences (all) | 46 | 83 | |
| Infections and infestations | | | |

| | | |
|-----------------------------|-------------------|-------------------|
| Bronchitis | | |
| subjects affected / exposed | 6 / 118 (5.08%) | 12 / 239 (5.02%) |
| occurrences (all) | 6 | 12 |
| Ear infection | | |
| subjects affected / exposed | 21 / 118 (17.80%) | 42 / 239 (17.57%) |
| occurrences (all) | 21 | 42 |
| Gastroenteritis | | |
| subjects affected / exposed | 32 / 118 (27.12%) | 61 / 239 (25.52%) |
| occurrences (all) | 32 | 61 |
| Pharyngitis | | |
| subjects affected / exposed | 5 / 118 (4.24%) | 14 / 239 (5.86%) |
| occurrences (all) | 5 | 14 |
| Respiratory tract infection | | |
| subjects affected / exposed | 11 / 118 (9.32%) | 17 / 239 (7.11%) |
| occurrences (all) | 11 | 17 |
| Rhinitis | | |
| subjects affected / exposed | 42 / 118 (35.59%) | 85 / 239 (35.56%) |
| occurrences (all) | 42 | 85 |
| Skin infection | | |
| subjects affected / exposed | 16 / 118 (13.56%) | 16 / 239 (6.69%) |
| occurrences (all) | 16 | 16 |
| Urinary tract infection | | |
| subjects affected / exposed | 8 / 118 (6.78%) | 3 / 239 (1.26%) |
| occurrences (all) | 8 | 3 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|---|
| 19 February 2008 | Amendment 1 was made in response to comments of the Ethics Committee of Mali and included the following changes: 1) Data and related publications on invasive pneumococcal disease in Mali were included; 2) Update on the presentation and administration of the OPV vaccine (Polio Sabin); 3) Update in the statistical analysis of safety; 4) Clarification on recording in the clinical report form (CRF) of administered vaccines other than the study vaccines; 5) Correction in the reference to the standard operating procedure (SOP) on destruction of used/unused vaccine vials/syringes/containers. |
| 17 March 2009 | Amendment 2 was made to include the following changes: 1) Planning of an interim analysis on all cleaned demographic, reactogenicity and immunogenicity data pertaining to Malian subjects enrolled by 31 December 2008; 2) Change in coordinating author and contributing authors. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported