



Clinical trial results:

A phase II, randomized, controlled, observer-blind study to assess the safety, reactogenicity and immunogenicity of two formulations of GlaxoSmithKline (GSK) Biologicals' Streptococcus pneumoniae protein containing vaccine given as a 3-dose primary vaccination course co-administered with DTPa-HBV-IPV/Hib* vaccine during the first 6 months of life and as a booster dose at 12-15 months of age.

*DTPa-HBV-IPV/Hib = Infanrix hexa™

Summary

| | |
|--------------------------|-----------------|
| EudraCT number | 2010-019730-27 |
| Trial protocol | CZ PL SE DE |
| Global end of trial date | 01 October 2012 |

Results information

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|--------------------------------|---------------|
| Result version number | v1 |
| This version publication date | 01 March 2016 |
| First version publication date | 04 April 2015 |

Trial information

Trial identification

| | |
|-----------------------|--------|
| Sponsor protocol code | 113994 |
|-----------------------|--------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01204658 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | GlaxoSmithKline Biologicals |
| Sponsor organisation address | Rue de l'Institut 89, Rixensart, Belgium, |
| Public contact | Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089904466, GSKClinicalSupportHD@gsk.com |
| Scientific contact | Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089904466, GSKClinicalSupportHD@gsk.com |

Notes:

Paediatric regulatory details

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|--|-----|
| 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 | Interim |
| Date of interim/final analysis | 25 November 2013 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 01 October 2012 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

1. Non-inferiority of the candidate pneumococcal vaccine (dPly-Low Dose [LD] and PhtD-LD)[10PP-LD] versus Synflorix™ vaccine when administered with Infanrix hexa™ (DTPa-HBV-IPV/Hib) as a 3-dose primary vaccination, in terms of post-primary immunization fever > 40.0°C (rectal temperature) with causal relationship to vaccination.

2. (sequential): Non-inferiority of the candidate pneumococcal vaccine (dPly-High Dose [HD] and PhtD-HD)[10PP-HD] versus Synflorix™ vaccine when administered with Infanrix hexa™ as a 3-dose primary vaccination, in terms of post-primary immunization fever > 40.0°C (rectal temperature) with causal relationship to vaccination.

Criteria = Non-inferiority supported if one can rule out an increase, in terms of percentage of subjects with fever >40.0°C with causal relationship to vaccination (10PP-LD or 10PP-HD group as compared to Synflorix™ group) above 5% + half the incidence in the control group (= null hypothesis) as shown by a one-sided P-value < 5%.

Protection of trial subjects:

GSK has monitored the study to verify that, amongst others, the:

- Data are authentic, accurate, and complete.
- Safety and rights of subjects are being protected.
- Study is conducted in accordance with the currently approved protocol and any amendments, any other study agreements, GCP and all applicable regulatory requirements.

All subjects were supervised after vaccination with appropriate medical treatment readily available.

Vaccines were administered by qualified and trained personnel. Only eligible subjects that had no contraindications to any components of the vaccines were vaccinated. Subjects were followed-up for 31 days after each/last vaccination.

Background therapy: -

Evidence for comparator: -

| | |
|---|-------------------|
| Actual start date of recruitment | 27 September 2010 |
| 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 | Poland: 110 |
| Country: Number of subjects enrolled | Sweden: 22 |
| Country: Number of subjects enrolled | Czech Republic: 434 |
| Country: Number of subjects enrolled | Germany: 10 |
| Worldwide total number of subjects | 576 |
| EEA total number of subjects | 576 |

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) | 576 |
| 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:

A total of 576 subjects were initially enrolled in the study. Of these, one subject was older than protocol defined age range for the first vaccination, and therefore did not receive any vaccination.

Pre-assignment

Screening details:

The study duration is approximately 10 to 14 months depending on age at recruitment and age at booster vaccination. 2 Phases in the study: Primary Phase when subjects received a 3-dose of pneumococcal vaccine co-administered with Infanrix hexa™ (Months 0, 1, 2), and Booster Phase when subjects received one dose of the same vaccines (Month 10).

Pre-assignment period milestones

| | |
|------------------------------|-----|
| Number of subjects started | 576 |
| Number of subjects completed | 575 |

Pre-assignment subject non-completion reasons

| | |
|----------------------------|---|
| Reason: Number of subjects | Study vaccine dose not administrated: 1 |
|----------------------------|---|

Period 1

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

Blinding implementation details:

Data collected in an observer-blind manner, meaning that during the course of the study, the subject and those responsible for the evaluation of any study endpoint (e.g. safety, reactogenicity, and immunogenicity) will all be unaware of which vaccine was administered. To do so, vaccine preparation and administration will be done by authorised medical personnel who will not participate in any of the study clinical evaluation assays.

The laboratory will be blinded to the treatment.

Arms

| | |
|------------------------------|-----------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | 10PP-LD/Infanrix hexa Group |

Arm description:

This group consisted in infants aged 6-14 weeks at primary vaccination who received a 3-dose primary vaccination of the GSK 2189242A (or 10PP) vaccine combined with low doses (LD) of pneumococcal pneumolysin toxoid proteins (dPly) and pneumococcal histidine protein D (PhtD) co-administered with the Infanrix hexa™ vaccine at Study Months 0, 1 and 2. Subjects also received a booster dose of each of these vaccines, administered at Study Month 10.

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | Pneumococcal vaccine GSK 2189242A (Low Dose formulation 1) |
| Investigational medicinal product code | GSK 2189242A LD |
| Other name | |
| Pharmaceutical forms | Suspension for injection in pre-filled syringe |
| Routes of administration | Intramuscular use |

Dosage and administration details:

4 doses: 3 primary doses at Study Months 0, 1 and 2. Subjects also received a booster dose , administered at Study Month 10. The 3 primary doses of the 10PP vaccine were administered intramuscularly (IM) in the thigh, on the right side. Booster doses were administered IM into the deltoid or thigh if the deltoid muscle size was not adequate, on the left side for the 10PP vaccine.

| | |
|--|--|
| Investigational medicinal product name | Infanrix hexa™ |
| Investigational medicinal product code | DTPa-HBV-IPV/Hib |
| Other name | |
| Pharmaceutical forms | Suspension for injection in pre-filled syringe |
| Routes of administration | Intramuscular use |

Dosage and administration details:

4 doses: 3 primary doses at Study Months 0, 1 and 2. Subjects also received a booster dose , administered at Study Month 10. The 3 primary doses of the Infanrix hexa™ vaccines were administered intramuscularly (IM) in the thigh, on the left side. Booster dose was administered IM into the deltoid or thigh if the deltoid muscle size was not adequate, on the right side.

| | |
|------------------|-----------------------------|
| Arm title | 10PP-HD/Infanrix hexa Group |
|------------------|-----------------------------|

Arm description:

This group consisted in infants aged 6-14 weeks at primary vaccination who received a 3-dose primary vaccination of the GSK 2189242A (or 10PP) vaccine combined with high doses (HD) of pneumococcal pneumolysin toxoid proteins (dPly) and pneumococcal histidine protein D (PhtD), co-administered with the Infanrix hexa™ vaccine at Study Months 0, 1 and 2. Subjects also received a booster dose of each of these vaccines, administered at Study Month 10.

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | Pneumococcal vaccine (High Dose formulation 2) |
| Investigational medicinal product code | GSK 2189242A HD |
| Other name | |
| Pharmaceutical forms | Suspension for injection in pre-filled syringe |
| Routes of administration | Intramuscular use |

Dosage and administration details:

4 doses: 3-dose primary vaccination at Study Months 0, 1 and 2 and a booster dose administered at Study Month 10. The 3 primary doses of the 10PP vaccine were administered intramuscularly (IM) in the thigh, on the right side. Booster dose was administered IM into the deltoid or thigh if the deltoid muscle size was not adequate, on the left side.

| | |
|--|--|
| Investigational medicinal product name | Infanrix hexa™ |
| Investigational medicinal product code | DTPa-HBV-IPV/Hib |
| Other name | |
| Pharmaceutical forms | Suspension for injection in pre-filled syringe |
| Routes of administration | Intramuscular use |

Dosage and administration details:

4 doses: 3 primary doses at Study Months 0, 1 and 2. Subjects also received a booster dose , administered at Study Month 10. The 3 primary doses of the Infanrix hexa™ vaccines were administered intramuscularly (IM) in the thigh, on the left side. Booster dose was administered IM into the deltoid or thigh if the deltoid muscle size was not adequate, on the right side.

| | |
|------------------|-------------------------------|
| Arm title | Synflorix/Infanrix hexa Group |
|------------------|-------------------------------|

Arm description:

This group consisted in infants aged 6-14 weeks at primary vaccination who received a 3-dose primary vaccination of Synflorix™ vaccine, co-administered with the Infanrix hexa™ vaccine at Study Months 0, 1 and 2. Subjects also received a booster dose of each of these vaccines, administered at Study Month 10.

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

Dosage and administration details:

4 doses: 3-dose primary vaccination at Study Months 0, 1 and 2 and a booster dose administered at Study Month 10. The 3 primary doses of Synflorix™ vaccine were administered intramuscularly (IM) in the thigh, on the right side. Booster dose was administered IM into the deltoid or thigh if the deltoid muscle size was not adequate, on the left side.

| | |
|--|--|
| Investigational medicinal product name | Infanrix hexa™ |
| Investigational medicinal product code | DTPa-HBV-IPV/Hib |
| Other name | |
| Pharmaceutical forms | Suspension for injection in pre-filled syringe |
| Routes of administration | Intramuscular use |

Dosage and administration details:

4 doses: 3 primary doses at Study Months 0, 1 and 2. Subjects also received a booster dose , administered at Study Month 10. The 3 primary doses of the Infanrix hexa™ vaccines were administered intramuscularly (IM) in the thigh, on the left side. Booster dose was administered IM into the deltoid or thigh if the deltoid muscle size was not adequate, on the right side.

| | |
|------------------|--------------------------------|
| Arm title | Prevnar 13/Infanrix hexa Group |
|------------------|--------------------------------|

Arm description:

This group consisted in infants aged 6-14 weeks at primary vaccination who received a 3-dose primary vaccination of Prevnar 13™ vaccine, co-administered with the Infanrix hexa™ vaccine at Study Months 0, 1 and 2. Subjects also received a booster dose of each of these vaccines, administered at Study Month 10.

| | |
|--|--|
| Arm type | Active comparator |
| Investigational medicinal product name | Prevenar 13™ |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection in pre-filled syringe |
| Routes of administration | Intramuscular use |

Dosage and administration details:

4 doses: 3-dose primary vaccination of Prevnar 13™ vaccine at Study Months 0, 1 and 2 and a booster dose , administered at Study Month 10. The 3 primary doses of Prevnar 13™ were administered intramuscularly (IM) in the thigh, on the right side. Booster dose was administered IM into the deltoid or thigh if the deltoid muscle size was not adequate, on the left side.

| | |
|--|--|
| Investigational medicinal product name | Infanrix hexa™ |
| Investigational medicinal product code | DTPa-HBV-IPV/Hib |
| Other name | |
| Pharmaceutical forms | Suspension for injection in pre-filled syringe |
| Routes of administration | Intramuscular use |

Dosage and administration details:

4 doses: 3 primary doses at Study Months 0, 1 and 2. Subjects also received a booster dose , administered at Study Month 10. The 3 primary doses of the Infanrix hexa™ vaccines were administered intramuscularly (IM) in the thigh, on the left side. Booster dose was administered IM into the deltoid or thigh if the deltoid muscle size was not adequate, on the right side.

| Number of subjects in period 1^[1] | 10PP-LD/Infanrix hexa Group | 10PP-HD/Infanrix hexa Group | Synflorix/Infanrix hexa Group |
|---|-----------------------------|-----------------------------|-------------------------------|
| Started | 146 | 142 | 145 |
| Completed | 144 | 140 | 140 |
| Not completed | 2 | 2 | 5 |
| Consent withdrawn by subject | 2 | 2 | 4 |
| Adverse event, non-fatal | - | - | 1 |

| Number of subjects in period 1^[1] | Prevnar 13/Infanrix hexa Group |
|---|--------------------------------|
| Started | 142 |
| Completed | 140 |
| Not completed | 2 |

| | |
|------------------------------|---|
| Consent withdrawn by subject | 2 |
| Adverse event, non-fatal | - |

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: A total of 576 subjects were initially enrolled in the study. Of these, one subject was older than protocol defined age range for the first vaccination, and therefore did not receive any vaccination.

Baseline characteristics

Reporting groups

| | |
|---|--------------------------------|
| Reporting group title | 10PP-LD/Infanrix hexa Group |
| Reporting group description: | |
| This group consisted in infants aged 6-14 weeks at primary vaccination who received a 3-dose primary vaccination of the GSK 2189242A (or 10PP) vaccine combined with low doses (LD) of pneumococcal pneumolysin toxoid proteins (dPly) and pneumococcal histidine protein D (PhtD) co-administered with the Infanrix hexa™ vaccine at Study Months 0, 1 and 2. Subjects also received a booster dose of each of these vaccines, administered at Study Month 10. | |
| Reporting group title | 10PP-HD/Infanrix hexa Group |
| Reporting group description: | |
| This group consisted in infants aged 6-14 weeks at primary vaccination who received a 3-dose primary vaccination of the GSK 2189242A (or 10PP) vaccine combined with high doses (HD) of pneumococcal pneumolysin toxoid proteins (dPly) and pneumococcal histidine protein D (PhtD), co-administered with the Infanrix hexa™ vaccine at Study Months 0, 1 and 2. Subjects also received a booster dose of each of these vaccines, administered at Study Month 10. | |
| Reporting group title | Synflorix/Infanrix hexa Group |
| Reporting group description: | |
| This group consisted in infants aged 6-14 weeks at primary vaccination who received a 3-dose primary vaccination of Synflorix™ vaccine, co-administered with the Infanrix hexa™ vaccine at Study Months 0, 1 and 2. Subjects also received a booster dose of each of these vaccines, administered at Study Month 10. | |
| Reporting group title | Prevnar 13/Infanrix hexa Group |
| Reporting group description: | |
| This group consisted in infants aged 6-14 weeks at primary vaccination who received a 3-dose primary vaccination of Prevnar 13™ vaccine, co-administered with the Infanrix hexa™ vaccine at Study Months 0, 1 and 2. Subjects also received a booster dose of each of these vaccines, administered at Study Month 10. | |

| Reporting group values | 10PP-LD/Infanrix hexa Group | 10PP-HD/Infanrix hexa Group | Synflorix/Infanrix hexa Group |
|---|-----------------------------|-----------------------------|-------------------------------|
| Number of subjects | 146 | 142 | 145 |
| Age categorical Units: Subjects | | | |
| In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over | | | |
| Age continuous Units: weeks | | | |
| arithmetic mean | 10.3 | 10.1 | 10.1 |
| standard deviation | ± 2.49 | ± 2.7 | ± 2.61 |
| Gender categorical Units: Subjects | | | |
| Female | 65 | 67 | 70 |
| Male | 81 | 75 | 75 |

| Reporting group values | Prevnar 13/Infanrix hexa Group | Total | |
|---|-----------------------------------|-------|--|
| Number of subjects | 142 | 575 | |
| 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 | 10.2 | | |
| standard deviation | ± 2.64 | - | |
| Gender categorical Units: Subjects | | | |
| Female | 66 | 268 | |
| Male | 76 | 307 | |

End points

End points reporting groups

| | |
|---|--------------------------------|
| Reporting group title | 10PP-LD/Infanrix hexa Group |
| Reporting group description: This group consisted in infants aged 6-14 weeks at primary vaccination who received a 3-dose primary vaccination of the GSK 2189242A (or 10PP) vaccine combined with low doses (LD) of pneumococcal pneumolysin toxoid proteins (dPly) and pneumococcal histidine protein D (PhtD) co-administered with the <i>Infanrix hexa</i> TM vaccine at Study Months 0, 1 and 2. Subjects also received a booster dose of each of these vaccines, administered at Study Month 10. | |
| Reporting group title | 10PP-HD/Infanrix hexa Group |
| Reporting group description: This group consisted in infants aged 6-14 weeks at primary vaccination who received a 3-dose primary vaccination of the GSK 2189242A (or 10PP) vaccine combined with high doses (HD) of pneumococcal pneumolysin toxoid proteins (dPly) and pneumococcal histidine protein D (PhtD), co-administered with the <i>Infanrix hexa</i> TM vaccine at Study Months 0, 1 and 2. Subjects also received a booster dose of each of these vaccines, administered at Study Month 10. | |
| Reporting group title | Synflorix/Infanrix hexa Group |
| Reporting group description: This group consisted in infants aged 6-14 weeks at primary vaccination who received a 3-dose primary vaccination of <i>Synflorix</i> TM vaccine, co-administered with the <i>Infanrix hexa</i> TM vaccine at Study Months 0, 1 and 2. Subjects also received a booster dose of each of these vaccines, administered at Study Month 10. | |
| Reporting group title | Prevnar 13/Infanrix hexa Group |
| Reporting group description: This group consisted in infants aged 6-14 weeks at primary vaccination who received a 3-dose primary vaccination of <i>Prevnar 13</i> TM vaccine, co-administered with the <i>Infanrix hexa</i> TM vaccine at Study Months 0, 1 and 2. Subjects also received a booster dose of each of these vaccines, administered at Study Month 10. | |

Primary: Number of subjects with any and Grade 3 solicited general symptoms and with solicited general symptoms related to vaccination – Primary Phase of the study

| | |
|--|---|
| End point title | Number of subjects with any and Grade 3 solicited general symptoms and with solicited general symptoms related to vaccination – Primary Phase of the study ^[1] |
| End point description: Assessed solicited general symptoms were Drowsiness, Irritability, Loss of appetite (Loss Appet.) and Fever (rectal temperature higher than or equal to [\geq] 38 degrees Celsius [$^{\circ}$ C]). Any = Occurrence of the specified solicited general symptom, regardless of intensity and relationship to vaccination. Related = Occurrence of the specified symptom assessed by the investigators as causally related to vaccination. Grade 3 (G3) Drowsiness = Drowsiness that prevented normal activity. G3 Irritability = Crying that could not be comforted/prevented normal activity. G3 Loss of appetite = Subject did not eat at all. G3 Fever = Rectal temperature higher than ($>$) 40.0 $^{\circ}$ C. Primary results correspond to results for occurrences of G3 fever symptoms assessed by the investigators as related to vaccination (Related G3 fever). | |
| End point type | Primary |
| End point timeframe: Within the 7-day (Days 0-6) periods post vaccination, after each dose (D) of the 3-dose primary vaccination course | |
| 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 scope of this primary end point was descriptive, no statistical hypothesis test was performed. | |

| End point values | 10PP- LD/Infanrix hexa Group | 10PP- HD/Infanrix hexa Group | Synflorix/Infan- rix hexa Group | Prev- nar 13/Infanrix hexa Group |
|--|------------------------------------|------------------------------------|------------------------------------|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 146 | 142 | 144 | 142 |
| Units: Subject | | | | |
| Any Drowsiness, post D1 (N=146;142;144;142) | 82 | 76 | 72 | 77 |
| G3 Drowsiness, post D1 (N=146;142;144;142) | 4 | 0 | 2 | 2 |
| Related Drowsiness, post D1 (N=146;142;144;142) | 63 | 58 | 52 | 58 |
| Any Irritability, post D1 (N=146;142;144;142) | 93 | 82 | 89 | 82 |
| G3 Irritability, post D1 (N=146;142;144;142) | 6 | 9 | 9 | 5 |
| Related Irritability, post D1 (N=146;142;144;142) | 70 | 62 | 66 | 57 |
| Any Loss Appet., post D1 (N=146;142;144;142) | 38 | 32 | 39 | 32 |
| G3 Loss Appet., post D1 (N=146;142;144;142) | 0 | 1 | 0 | 0 |
| Related Loss Appet., post D1 (N=146;142;144;142) | 28 | 26 | 29 | 21 |
| Any Fever, post D1 (N=146;142;144;142) | 45 | 32 | 53 | 28 |
| G3 Fever, post D1 (N=146;142;144;142) | 0 | 0 | 0 | 0 |
| Related Fever, post D1 (N=146;142;144;142) | 33 | 25 | 44 | 27 |
| Related G3 Fever, post D1 (N=146;142;144;142) | 0 | 0 | 0 | 0 |
| Any Drowsiness, post D2 (N=146;142;144;142) | 71 | 63 | 70 | 66 |
| G3 Drowsiness, post D2 (N=146;142;144;142) | 4 | 2 | 1 | 1 |
| Related Drowsiness, post D2 (N=146;142;144;142) | 53 | 49 | 56 | 55 |
| Any Irritability, post D2 (N=146;142;144;142) | 88 | 81 | 86 | 87 |
| G3 Irritability, post D2 (N=146;142;144;142) | 8 | 3 | 5 | 6 |
| Related Irritability, post D2 (N=146;142;144;142) | 69 | 66 | 66 | 67 |
| Any Loss Appet., post D2 (N=146;142;144;142) | 32 | 30 | 28 | 30 |
| G3 Loss Appet., post D2 (N=146;142;144;142) | 1 | 2 | 0 | 0 |
| Related Loss Appet., post D2 (N=146;142;144;142) | 23 | 21 | 18 | 25 |
| Any Fever, post D2 (N=146;142;144;142) | 40 | 50 | 38 | 38 |
| G3 Fever, post D2 (N=146;142;144;142) | 0 | 0 | 0 | 0 |
| Related Fever, post D2 (N=146;142;144;142) | 32 | 39 | 33 | 31 |
| Related G3 Fever, post D2 (N=146;142;144;142) | 0 | 0 | 0 | 0 |
| Any Drowsiness, post D3 (N=146;141;143;142) | 57 | 48 | 56 | 48 |
| Grade 3 Drowsiness, post D3 (N=146;141;143;142) | 2 | 0 | 1 | 1 |

| | | | | |
|--|----|----|----|----|
| Related Drowsiness, post D3 (N=146;141;143;142) | 51 | 38 | 44 | 36 |
| Any Irritability, post D3 (N=146;141;143;142) | 62 | 73 | 62 | 72 |
| G3 Irritability, post D3 (N=146;141;143;142) | 7 | 1 | 3 | 2 |
| Related Irritability, post D3 (N=146;141;143;142) | 52 | 55 | 48 | 53 |
| Any Loss Appet., post D3 (N=146,141,143,142) | 28 | 25 | 24 | 21 |
| G3 Loss Appet., post D3 (N=146,141,143,142) | 0 | 0 | 2 | 2 |
| Related Loss Appet., post D3 (N=146,141,143,142) | 22 | 20 | 18 | 13 |
| Any Fever, post D3 (N=146;141;143;142) | 28 | 23 | 27 | 30 |
| G3 Fever, post D3 (N=146;141;143;142) | 0 | 0 | 0 | 0 |
| Related Fever, post D3 (N=146;141;143;142) | 23 | 19 | 20 | 22 |
| Related G3 Fever, post D3 (N=146;141;143;142) | 0 | 0 | 0 | 0 |

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects reporting fever > 40.0°C with causal relationship to vaccination after each primary vaccination dose and across doses in 10PP-LD/Infanrix hexa group and in Synflorix/Infanrix hexa group

| | |
|-----------------|---|
| End point title | Number of subjects reporting fever > 40.0°C with causal relationship to vaccination after each primary vaccination dose and across doses in 10PP-LD/Infanrix hexa group and in Synflorix/Infanrix hexa group ^[2] |
|-----------------|---|

End point description:

Grade 3 fever was defined as fever by rectal measurement >40.0°C. Related was defined a causal relationship to vaccination. This endpoint was assessed after each primary vaccination dose and across doses and in subjects in the 10PP-LD/Infanrix hexa (or 10PP-LD) and Synflorix/Infanrix hexa (or 10PN) groups only.

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

End point timeframe:

during the 7-day (Days 0-6) post-vaccination period following each primary vaccination dose and across doses

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This endpoint is related to the difference between 2 groups: the 10PP-LD/Infanrix hexa group and the Synflorix/Infanrix hexa group.

| End point values | 10PP-LD/Infanrix hexa Group | Synflorix/Infanrix hexa Group | | |
|-----------------------------|-----------------------------|-------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 146 | 144 | | |
| Units: percentage | | | | |
| number (not applicable) | | | | |

| | | | | |
|---|---|---|--|--|
| Fever > 40.0°C & Related Dose 1 (N=146, 144) | 0 | 0 | | |
| Fever> 40.0°C & Related Dose 2 (N=146, 144) | 0 | 0 | | |
| Fever> 40.0°C & Related Dose 3 (N=146, 143) | 0 | 0 | | |
| Fever> 40.0°C & Related across doses (N=146,144) | 0 | 0 | | |

Statistical analyses

| Statistical analysis title | Non-inferiority: 10PP-LD versus Synflorix - dose 1 |
|--|---|
| Statistical analysis description: | |
| Non-inferiority of 10PP-LD vaccine vs Synflorix™ vaccine post dose 1 was assessed by computing the difference in percentages of subjects reporting Grade 3 fever causally related to dose 1 vaccination in the 10PP-LD Group minus 10PN Group. Non-inferiority was supported if one could rule out an increase in terms of percentage of subjects (10PP-LD Group minus 10PN Group) above 5% + half the incidence in the 10PN Group (= null hypothesis) as shown by a 1-sided P-value < 5%. | |
| Comparison groups | Synflorix/Infanrix hexa Group v 10PP-LD/Infanrix hexa Group |
| Number of subjects included in analysis | 290 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | = 0.003 ^[3] |
| Method | Kem Phillip's statistical test |
| Parameter estimate | Difference in percentage |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.61 |
| upper limit | 2.57 |

Notes:

[3] - 1-sided P-value computed using Kem Philips'approach for ruling out an increase in % subjects with fever > 40.0°C and causal relationship to vaccination > the boundary expressed as 5% + 0.5*rate in the 10PN group.

| Statistical analysis title | Non-inferiority: 10PP-LD versus Synflorix - dose 2 |
|---|---|
| Statistical analysis description: | |
| Non-inferiority of 10PP-LD vaccine vs Synflorix™ vaccine post dose 2 was assessed by computing the difference in percentages of subjects reporting Grade 3 fever causally related to dose 2 vaccination in the 10PP-LD Group minus 10PN Group. Non-inferiority was supported if one could rule out an increase in terms of percentage of subjects (10PP-LD Group minus 10PN Group) above 5% + half the incidence in the 10PN Group (= null hypothesis) as shown by a 1-sided P-value < 5% | |
| Comparison groups | Synflorix/Infanrix hexa Group v 10PP-LD/Infanrix hexa Group |
| Number of subjects included in analysis | 290 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | = 0.003 ^[4] |
| Method | Kem Phillip's statistical test |
| Parameter estimate | Difference in percentage |
| Point estimate | 0 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.61 |
| upper limit | 2.57 |

Notes:

[4] - 1-sided P-value computed using Kem Phillips'approach for ruling out an increase in % subjects with fever > 40.0°C and causal relationship to vaccination > the boundary expressed as 5% + 0.5*rate in the 10PN group.

| | |
|-----------------------------------|--|
| Statistical analysis title | Non-inferiority: 10PP-LD versus Synflorix - dose 3 |
|-----------------------------------|--|

Statistical analysis description:

Non-inferiority of 10PP-LD vaccine vs Synflorix™ vaccine post dose 3 was assessed by computing the difference in percentages of subjects reporting Grade 3 fever causally related to dose 3 vaccination in the 10PP-LD Group minus 10PN Group. Non-inferiority was supported if one could rule out an increase in terms of percentage of subjects (10PP-LD Group minus 10PN Group) above 5% + half the incidence in the 10PN Group (= null hypothesis) as shown by a 1-sided P-value < 5%

| | |
|---|---|
| Comparison groups | Synflorix/Infanrix hexa Group v 10PP-LD/Infanrix hexa Group |
| Number of subjects included in analysis | 290 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | = 0.003 ^[5] |
| Method | Kem Phillip's statistical test |
| Parameter estimate | Difference in percentage |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.62 |
| upper limit | 2.57 |

Notes:

[5] - 1-sided P-value computed using Kem Phillips'approach for ruling out an increase in % subjects with fever > 40.0°C and causal relationship to vaccination > the boundary expressed as 5% + 0.5*rate in the 10PN group.

| | |
|-----------------------------------|--|
| Statistical analysis title | Non-inferiority:10PP-LD vs Synflorix - across dose |
|-----------------------------------|--|

Statistical analysis description:

Non-inferiority of 10PP-LD vaccine vs Synflorix™ vaccine across doses was assessed by computing the difference in percentages of subjects reporting Grade 3 fever causally related to vaccination, across doses, in the 10PP-LD Group minus 10PN Group. Non-inferiority was supported if one could rule out an increase in terms of percentage of subjects (10PP-LD Group minus 10PN Group) above 5% + half the incidence in the 10PN Group (= null hypothesis) as shown by a 1-sided P-value < 5%

| | |
|---|---|
| Comparison groups | Synflorix/Infanrix hexa Group v 10PP-LD/Infanrix hexa Group |
| Number of subjects included in analysis | 290 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | = 0.003 ^[6] |
| Method | Kem Phillip's statistical test |
| Parameter estimate | Difference in percentage |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.61 |
| upper limit | 2.57 |

Notes:

[6] - 1-sided P-value computed using Kem Philips'approach for ruling out an increase in % subjects with fever > 40.0°C and causal relationship to vaccination > the boundary expressed as 5% + 0.5*rate in the 10PN group.

Primary: Number of subjects reporting fever > 40° C with causal relationship to vaccination after each primary vaccination dose and across doses in the 10PP-HD/Infanrix hexa group and in the Synflorix/Infanrix hexa group

| | |
|-----------------|--|
| End point title | Number of subjects reporting fever > 40° C with causal relationship to vaccination after each primary vaccination dose and across doses in the 10PP-HD/Infanrix hexa group and in the Synflorix/Infanrix hexa group ^[7] |
|-----------------|--|

End point description:

Grade 3 fever was defined as fever by rectal measurement >40.0°C. Related was defined a causal relationship to vaccination. This endpoint was assessed after each primary vaccination dose and across doses and in subjects in the 10PP-HD/Infanrix hexa (or 10PP-HD) and Synflorix/Infanrix hexa (or 10PN) groups only.

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

End point timeframe:

during the 7-day (Days 0-6) post-vaccination period following each primary vaccination dose and across doses

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This endpoint is related to the difference between 2 groups: the 10PP-HD/Infanrix hexa group and the Synflorix/Infanrix hexa group.

| End point values | 10PP-HD/Infanrix hexa Group | Synflorix/Infanrix hexa Group | | |
|--|-----------------------------|-------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 142 | 144 | | |
| Units: percentage | | | | |
| number (not applicable) | | | | |
| Fever > 40.0°C & Related Dose 1 (N=142,144) | 0 | 0 | | |
| Fever> 40.0°C & Related Dose 2 (N=142,144) | 0 | 0 | | |
| Fever> 40.0°C & Related Dose 3 (N=141,143) | 0 | 0 | | |
| Fever> 40.0°C & Related across doses (N=142,144) | 0 | 0 | | |

Statistical analyses

| | |
|----------------------------|---|
| Statistical analysis title | Non-inferiority: 10PP-HD versus Synflorix- dose 1 |
|----------------------------|---|

Statistical analysis description:

Non-inferiority of 10PP-HD vaccine vs Synflorix™ vaccine post dose 1 was assessed by computing the difference in percentages of subjects reporting Grade 3 fever causally related to dose 1 vaccination in the 10PP-HD Group minus 10PN Group. Non-inferiority was supported if one could rule out an increase in terms of percentage of subjects (10PP-HD Group minus 10PN Group) above 5% + half the incidence in the 10PN Group (= null hypothesis) as shown by a 1-sided P-value < 5%.

| | |
|-------------------|---|
| Comparison groups | 10PP-HD/Infanrix hexa Group v Synflorix/Infanrix hexa Group |
|-------------------|---|

| | |
|---|-------------------------------|
| Number of subjects included in analysis | 286 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | = 0.003 ^[8] |
| Method | Kem Philips' statistical test |
| Parameter estimate | Difference in percentage |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.61 |
| upper limit | 2.64 |

Notes:

[8] - 1-sided P-value computed using Kem Philips' approach for ruling out an increase in % of subjects with fever > 40.0°C and causal relationship to vaccination above the boundary expressed as 5% + 0.5 *rate in the 10PN group.

| | |
|-----------------------------------|---|
| Statistical analysis title | Non-inferiority: 10PP-HD versus Synflorix- dose 2 |
|-----------------------------------|---|

Statistical analysis description:

Non-inferiority of 10PP-HD vaccine vs Synflorix™ vaccine post dose 2 was assessed by computing the difference in percentages of subjects reporting Grade 3 fever causally related to dose 2 vaccination in the 10PP-HD Group minus 10PN Group. Non-inferiority was supported if one could rule out an increase in terms of percentage of subjects (10PP-HD Group minus 10PN Group) above 5% + half the incidence in the 10PN Group (= null hypothesis) as shown by a 1-sided P-value < 5%.

| | |
|---|---|
| Comparison groups | 10PP-HD/Infanrix hexa Group v Synflorix/Infanrix hexa Group |
| Number of subjects included in analysis | 286 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | = 0.003 ^[9] |
| Method | Kem Philips' statistical test |
| Parameter estimate | Difference in percentage |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.61 |
| upper limit | 2.64 |

Notes:

[9] - 1-sided P-value computed using Kem Philips' approach for ruling out an increase in % of subjects with fever > 40.0°C and causal relationship to vaccination above the boundary expressed as 5% + 0.5 *rate in the 10PN group.

| | |
|-----------------------------------|--|
| Statistical analysis title | Non-inferiority: 10PP-HD versus Synflorix - dose 3 |
|-----------------------------------|--|

Statistical analysis description:

Non-inferiority of 10PP-HD vaccine vs Synflorix™ vaccine post dose 3 was assessed by computing the difference in percentages of subjects reporting Grade 3 fever causally related to dose 3 vaccination in the 10PP-HD Group minus 10PN Group. Non-inferiority was supported if one could rule out an increase in terms of percentage of subjects (10PP-HD Group minus 10PN Group) above 5% + half the incidence in the 10PN Group (= null hypothesis) as shown by a 1-sided P-value < 5%.

| | |
|-------------------|---|
| Comparison groups | 10PP-HD/Infanrix hexa Group v Synflorix/Infanrix hexa Group |
|-------------------|---|

| | |
|---|-------------------------------|
| Number of subjects included in analysis | 286 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | = 0.003 ^[10] |
| Method | Kem Philips' statistical test |
| Parameter estimate | Difference in percentage |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.63 |
| upper limit | 2.66 |

Notes:

[10] - 1-sided P-value computed using Kem Philips'approach for ruling out an increase in % of subjects with fever > 40.0°C and causal relationship to vaccination above the boundary expressed as 5% + 0.5 *rate in the 10PN group.

| | |
|-----------------------------------|--|
| Statistical analysis title | Non-inferiority: 10PP-HD vs Synflorix-across doses |
|-----------------------------------|--|

Statistical analysis description:

Non-inferiority of 10PP-HD vaccine vs Synflorix™ vaccine across doses was assessed by computing the difference in percentages of subjects reporting Grade 3 fever causally related to vaccination, across doses, in the 10PP-HD Group minus 10PN Group. Non-inferiority was supported if one could rule out an increase in terms of percentage of subjects (10PP-HD Group minus 10PN Group) above 5% + half the incidence in the 10PN Group (= null hypothesis) as shown by a 1-sided P-value < 5%.

| | |
|---|---|
| Comparison groups | 10PP-HD/Infanrix hexa Group v Synflorix/Infanrix hexa Group |
| Number of subjects included in analysis | 286 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | = 0.003 ^[11] |
| Method | Kem Philips' statistical test |
| Parameter estimate | Difference in percentage |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.61 |
| upper limit | 2.64 |

Notes:

[11] - 1-sided P-value computed using Kem Philips'approach for ruling out an increase in % of subjects with fever > 40.0°C and causal relationship to vaccination above the boundary expressed as 5% + 0.5 *rate in the 10PN group.

Secondary: Antibody concentrations against pneumococcal pneumolysin toxoid (dPly) and pneumococcal histidine triad protein D (PhtD) proteins – Primary Phase of the study.

| | |
|-----------------|---|
| End point title | Antibody concentrations against pneumococcal pneumolysin toxoid (dPly) and pneumococcal histidine triad protein D (PhtD) proteins – Primary Phase of the study. |
|-----------------|---|

End point description:

Antibody concentrations against dPly and PhtD (anti-dPly and anti-PhtD, respectively) were measured by enzyme-linked immunosorbent assay (ELISA), expressed as geometric mean concentrations (GMCs), in ELISA Units per milliliter (EL.U/mL). Cut-offs for seropositivity were concentrations higher than or equal to (≥)12 EL.U/mL for anti-dPly antibodies and ≥ 17 EL.U/mL for anti-PhtD antibodies. This outcome concerns results for the Primary Phase of the study.

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

End point timeframe:

At Month 3, e. g. one month post-Dose 3 of pneumococcal vaccine (10PP, Synflorix™ or Prevnar 13™)

| End point values | 10PP-LD/Infanrix hexa Group | 10PP-HD/Infanrix hexa Group | Synflorix/Infanrix hexa Group | Prenar 13/Infanrix hexa Group |
|--|----------------------------------|------------------------------------|-------------------------------|-------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 131 | 134 | 136 | 133 |
| Units: EL.U/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-dPly – At Month 3 | 9501.35 (8260.68 to 10928.37) | 12067.41 (10582.51 to 13760.66) | 459.97 (398.31 to 531.18) | 477.31 (409 to 557.03) |
| Anti-PhtD – At Month 3 | 1495.15 (1274.28 to 1754.29) | 1986.96 (1726.88 to 2286.21) | 523.61 (453.71 to 604.28) | 555 (473.15 to 651.02) |

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations against protein D (anti-PD) – Primary Phase of the study.

| | |
|-----------------|---|
| End point title | Antibody concentrations against protein D (anti-PD) – Primary Phase of the study. |
|-----------------|---|

End point description:

Antibody concentrations were measured by enzyme-linked immunosorbent assay (ELISA), expressed as geometric mean concentrations (GMCs), in ELISA Units per milliliter (EL.U/mL). The seropositivity cut-off of the assay was a concentration of anti-PD antibodies ≥ 100 EL.U/mL. This outcome concerns results for the Primary Phase of the study.

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

End point timeframe:

At Month 3, e. g. one month post-Dose 3 of pneumococcal vaccine (10PP, Synflorix™ or Prevnar 13™)

| End point values | 10PP-LD/Infanrix hexa Group | 10PP-HD/Infanrix hexa Group | Synflorix/Infanrix hexa Group | Prenar 13/Infanrix hexa Group |
|--|-----------------------------|-----------------------------|-------------------------------|-------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 133 | 134 | 137 | 134 |
| Units: EL.U/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-PD – At Month 3 | 1135.7 (929.3 to 1388) | 1337.3 (1109.2 to 1612.2) | 1539 (1258.4 to 1882.1) | 149.6 (114.2 to 195.9) |

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations against pneumococcal serotypes – Primary Phase of the study.

| | |
|-----------------|--|
| End point title | Antibody concentrations against pneumococcal serotypes – Primary Phase of the study. |
|-----------------|--|

End point description:

Antibodies assessed for this outcome measure were those against the vaccine/cross-reactive pneumococcal serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F and 23F (ANTI-1, -3, -4, -5, -6A, -6B, -7F, -9V, -14, -18C, -19A, -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.

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

End point timeframe:

At Month 3, e. g. one month post-Dose 3 of pneumococcal vaccine (10PP, Synflorix™ or Prevnar 13™)

| End point values | 10PP-LD/Infanrix hexa Group | 10PP-HD/Infanrix hexa Group | Synflorix/Infanrix hexa Group | Prevnar 13/Infanrix hexa Group |
|--|-----------------------------|-----------------------------|-------------------------------|--------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 133 | 135 | 137 | 134 |
| Units: µg/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| ANTI-1 At Month 3 (N=132,131,134,134) | 1.56 (1.36 to 1.79) | 1.59 (1.37 to 1.84) | 1.49 (1.28 to 1.74) | 2.18 (1.84 to 2.57) |
| ANTI-4 At Month 3 (N=132,133,133,134) | 2.04 (1.74 to 2.39) | 2.12 (1.83 to 2.44) | 1.82 (1.55 to 2.14) | 2.41 (2.04 to 2.85) |
| ANTI-5 At Month 3 (N=133,134,134,134) | 2.46 (2.13 to 2.85) | 2.56 (2.24 to 2.94) | 2.31 (2 to 2.67) | 2.78 (2.29 to 3.39) |
| ANTI-6B At Month 3 (N=131,129,133,134) | 0.37 (0.29 to 0.46) | 0.37 (0.31 to 0.45) | 0.4 (0.32 to 0.51) | 0.45 (0.36 to 0.56) |
| ANTI-7F At Month 3 (N=131,131,134,134) | 2.12 (1.86 to 2.41) | 2.21 (1.97 to 2.48) | 2.2 (1.92 to 2.5) | 2.93 (2.5 to 3.43) |
| ANTI-9V At Month 3 (N=133,135,137,134) | 1.83 (1.59 to 2.11) | 1.95 (1.73 to 2.21) | 1.99 (1.72 to 2.3) | 2.32 (1.96 to 2.75) |
| ANTI-14 At Month 3 (N=133,133,135,134) | 3.6 (3.11 to 4.17) | 3.71 (3.3 to 4.18) | 3.91 (3.41 to 4.48) | 4.14 (3.38 to 5.06) |
| ANTI-18C At Month 3 (N=133,132,135,134) | 2.27 (1.93 to 2.67) | 2.21 (1.87 to 2.62) | 2.45 (2.04 to 2.95) | 2.56 (2.14 to 3.06) |
| ANTI-19F At Month 3 (N=133,132,135,134) | 4.29 (3.64 to 5.07) | 4.13 (3.52 to 4.84) | 4.51 (3.79 to 5.36) | 3.47 (2.92 to 4.13) |
| ANTI-23F At Month 3 (N=132,133,135,134) | 0.66 (0.54 to 0.81) | 0.62 (0.5 to 0.78) | 0.67 (0.54 to 0.82) | 1.48 (1.17 to 1.87) |
| ANTI-3 (At Month 3 (N=131,129,132,134) | 0.05 (0.04 to 0.07) | 0.06 (0.05 to 0.07) | 0.05 (0.05 to 0.06) | 2.43 (2.05 to 2.89) |

| | | | | |
|--|---------------------|---------------------|---------------------|---------------------|
| ANTI-6A At Month 3 (N=130,132,133,134) | 0.13 (0.1 to 0.16) | 0.11 (0.09 to 0.14) | 0.11 (0.09 to 0.14) | 2.06 (1.7 to 2.5) |
| ANTI-19A At Month 3 (N=131,129,134,134) | 0.18 (0.14 to 0.22) | 0.17 (0.14 to 0.21) | 0.16 (0.13 to 0.2) | 2.75 (2.33 to 3.25) |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any and Grade 3 solicited local symptoms – Primary Phase of the study

| | |
|-----------------|---|
| End point title | Number of subjects with any and Grade 3 solicited local symptoms – Primary Phase of the study |
|-----------------|---|

End point description:

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

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

End point timeframe:

Within the 7-day (Days 0-6) periods post vaccination, after each dose (D) of the 3-dose primary vaccination course

| End point values | 10PP-LD/Infanrix hexa Group | 10PP-HD/Infanrix hexa Group | Synflorix/Infanrix hexa Group | Prevnar 13/Infanrix hexa Group |
|--|-----------------------------|-----------------------------|-------------------------------|--------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 146 | 142 | 144 | 142 |
| Units: Subject | | | | |
| Any Pain, post D1 (N=146;142;144;142) | 52 | 46 | 53 | 40 |
| Grade 3 Pain, post D1 (N=146;142;144;142) | 0 | 2 | 3 | 0 |
| Any Redness, post D1 (N=146;142;144;142) | 59 | 58 | 52 | 51 |
| Grade 3 Redness, post D1 (N=146;142;144;142) | 0 | 0 | 3 | 2 |
| Any Swelling, post D1 (N=146;142;144;142) | 47 | 46 | 34 | 37 |
| Grade 3 Swelling, post D1 (N=146;142;144;142) | 3 | 5 | 3 | 6 |
| Any Pain, post D2 (N=146;142;144;142) | 52 | 49 | 42 | 43 |
| Grade 3 Pain, post D2 (N=146;142;144;142) | 2 | 0 | 1 | 2 |
| Any Redness, post D2 (N=146;142;144;142) | 67 | 67 | 63 | 59 |
| Grade 3 Redness, post D2 (N=146;142;144;142) | 2 | 2 | 3 | 0 |
| Any Swelling, post D2 (N=146;142;144;142) | 49 | 56 | 43 | 38 |
| Grade 3 Swelling, post D2 (N=146;142;144;142) | 5 | 4 | 2 | 3 |

| | | | | |
|--|----|----|----|----|
| Any Pain, post D3 (N=146;141;143;142) | 41 | 35 | 37 | 45 |
| Grade 3 Pain, post D3 (N=146;141;143;142) | 2 | 3 | 1 | 1 |
| Any Redness, post D3 (N=146;141;143;142) | 65 | 65 | 58 | 65 |
| Grade 3 Redness, post D3 (N=146;141;143;142) | 3 | 2 | 0 | 3 |
| Any Swelling, post D3 (N=146;141;143;142) | 52 | 52 | 43 | 43 |
| Grade 3 Swelling, post D3 (N=146;141;143;142) | 6 | 3 | 3 | 5 |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any and Grade 3 solicited local symptoms – Booster Phase of the study

| | |
|--|---|
| End point title | Number of subjects with any and Grade 3 solicited local symptoms – Booster Phase of the study |
| End point description: Assessed local symptoms were pain, redness and swelling at injection site. Any = Occurrence of the specified solicited local symptom, regardless of intensity. Grade 3 Pain = Crying when limb was moved/spontaneously painful. Grade 3 Redness/Swelling = Redness/swelling at injection site larger than (>) 30 millimeters (mm). | |
| End point type | Secondary |
| End point timeframe: Within the 7-day (Days 0-6) period after booster vaccination | |

| End point values | 10PP-LD/Infanrix hexa Group | 10PP-HD/Infanrix hexa Group | Synflorix/Infanrix hexa Group | Prevnar 13/Infanrix hexa Group |
|--------------------------------------|-----------------------------|-----------------------------|-------------------------------|--------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 144 | 140 | 139 | 140 |
| Units: Subject | | | | |
| Any Pain, (N=144;140;139;140) | 77 | 73 | 61 | 68 |
| Grade 3 Pain (N=144;140;139;140) | 7 | 6 | 3 | 4 |
| Any Redness (N=144;140;139;140) | 83 | 81 | 68 | 66 |
| Grade 3 Redness (N=144;140;139;140) | 11 | 15 | 12 | 7 |
| Any Swelling (N=144;140;139;140) | 70 | 55 | 49 | 59 |
| Grade 3 Swelling (N=144;140;139;140) | 8 | 8 | 7 | 10 |

Statistical analyses

No statistical analyses for this end point

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

solicited general symptoms with relationship to vaccination – Booster Phase of the study

| | |
|-----------------|--|
| End point title | Number of subjects with any, Grade 3 solicited general symptoms and solicited general symptoms with relationship to vaccination – Booster Phase of the study |
|-----------------|--|

End point description:

Assessed solicited general symptoms were Drowsiness, Irritability, Loss of appetite (Loss Appet.) and Fever (rectal temperature higher than \geq 38 degrees Celsius [$^{\circ}$ C]). Any = Occurrence of the specified solicited general symptom, regardless of intensity and relationship to vaccination. Related = Occurrence of the specified symptom assessed by the investigator as causally related to vaccination. Grade 3 (G3) Drowsiness = Drowsiness that prevented normal activity. Grade 3 Irritability = Crying that could not be comforted/prevented normal activity. Grade 3 Loss of appetite = Subject did not eat at all. Grade 3 Fever = Axillary temperature higher than ($>$) 40.0 $^{\circ}$ C.

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

End point timeframe:

Within the 7-day (Days 0-6) period post vaccination after booster vaccination

| End point values | 10PP-LD/Infanrix hexa Group | 10PP-HD/Infanrix hexa Group | Synflorix/Infanrix hexa Group | Prevnar 13/Infanrix hexa Group |
|--|-----------------------------|-----------------------------|-------------------------------|--------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 144 | 140 | 139 | 140 |
| Units: Subject | | | | |
| Any Drowsiness (N=144;140;139;140) | 77 | 64 | 66 | 73 |
| G3 Drowsiness (N=144;140;139;140) | 1 | 5 | 1 | 1 |
| Related Drowsiness (N=144;140;139;140) | 68 | 61 | 59 | 69 |
| Any Irritability (N=144;140;139;140) | 95 | 84 | 82 | 90 |
| G3 Irritability (N=144;140;139;140) | 12 | 8 | 4 | 8 |
| Related Irritability (N=144;140;139;140) | 86 | 82 | 76 | 83 |
| Any Loss Appet. (N=144;140;139;140) | 49 | 38 | 36 | 57 |
| G3 Loss Appet. (N=144;140;139;140) | 3 | 4 | 2 | 2 |
| Related Loss Appet. (N=144;140;139;140) | 42 | 38 | 33 | 49 |
| Any Fever (N=144;140;139;140) | 50 | 55 | 51 | 53 |
| G3 Fever (N=144;140;139;140) | 1 | 0 | 1 | 3 |
| Related Fever (N=144;140;139;140) | 44 | 52 | 45 | 47 |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with unsolicited adverse events (AEs) – Primary Phase of the study

| | |
|-----------------|---|
| End point title | Number of subjects with unsolicited adverse events (AEs) – Primary Phase of the study |
|-----------------|---|

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 | 10PP-LD/Infanrix hexa Group | 10PP-HD/Infanrix hexa Group | Synflorix/Infanrix hexa Group | Prevnar 13/Infanrix hexa Group |
|-----------------------------|-----------------------------|-----------------------------|-------------------------------|--------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 146 | 142 | 145 | 142 |
| Units: Subject | | | | |
| Any AE | 55 | 68 | 64 | 61 |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with unsolicited adverse events (AEs) – Booster Phase of the study

| | |
|-----------------|---|
| End point title | Number of subjects with unsolicited adverse events (AEs) – Booster Phase of the study |
|-----------------|---|

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 | 10PP-LD/Infanrix hexa Group | 10PP-HD/Infanrix hexa Group | Synflorix/Infanrix hexa Group | Prevnar 13/Infanrix hexa Group |
|-----------------------------|-----------------------------|-----------------------------|-------------------------------|--------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 144 | 140 | 140 | 140 |
| Units: Subject | | | | |
| Any AE | 40 | 26 | 27 | 34 |

Statistical analyses

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited symptoms: during the 7 days post-primary vaccination and post-booster vaccination.

Unsolicited AEs during 31 days post-primary vaccination and post booster vaccination. SAEs: during the entire study period (Months 0-11).

Adverse event reporting additional description:

Solicited symptoms results are presented only for subjects for whom results were available. SAEs are not presented (n affected = 0): Detailed data are blinded as the study is still ongoing. Note: the occurrences (all) numbers were not calculated during the analysis: data entered are equal to the subject affected numbers.

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

Dictionary used

| | |
|--------------------|--------|
| Dictionary name | MedDRA |
| Dictionary version | 17 |

Reporting groups

| | |
|-----------------------|-----------------------------|
| Reporting group title | 10PP-LD/Infanrix hexa Group |
|-----------------------|-----------------------------|

Reporting group description:

This group consisted in infants aged 6-14 weeks at primary vaccination who received a 3-dose primary vaccination of the GSK 2189242A (or 10PP) vaccine combined with low doses (LD) of pneumococcal pneumolysin toxoid proteins (dPly) and pneumococcal histidine protein D (PhtD) co-administered with the *Infanrix hexa*[™] vaccine at Study Months 0, 1 and 2. Subjects also received a booster dose of each of these vaccines, administered at Study Month 10.

| | |
|-----------------------|-----------------------------|
| Reporting group title | 10PP-HD/Infanrix hexa Group |
|-----------------------|-----------------------------|

Reporting group description:

This group consisted in infants aged 6-14 weeks at primary vaccination who received a 3-dose primary vaccination of the GSK 2189242A (or 10PP) vaccine combined with high doses (HD) of pneumococcal pneumolysin toxoid proteins (dPly) and pneumococcal histidine protein D (PhtD), co-administered with the *Infanrix hexa*[™] vaccine at Study Months 0, 1 and 2. Subjects also received a booster dose of each of these vaccines, administered at Study Month 10.

| | |
|-----------------------|-------------------------------|
| Reporting group title | Synflorix/Infanrix hexa Group |
|-----------------------|-------------------------------|

Reporting group description:

This group consisted in infants aged 6-14 weeks at primary vaccination who received a 3-dose primary vaccination of *Synflorix*[™] vaccine, co-administered with the *Infanrix hexa*[™] vaccine at Study Months 0, 1 and 2. Subjects also received a booster dose of each of these vaccines, administered at Study Month 10.

| | |
|-----------------------|-------------------------------|
| Reporting group title | Pevnar 13/Infanrix hexa Group |
|-----------------------|-------------------------------|

Reporting group description:

This group consisted in infants aged 6-14 weeks at primary vaccination who received a 3-dose primary vaccination of *Pevnar 13*[™] vaccine, co-administered with the *Infanrix hexa*[™] vaccine at Study Months 0, 1 and 2. Subjects also received a booster dose of each of these vaccines, administered at Study Month 10.

| Serious adverse events | 10PP-LD/Infanrix hexa Group | 10PP-HD/Infanrix hexa Group | Synflorix/Infanrix hexa Group |
|---|-----------------------------|-----------------------------|-------------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 146 (0.00%) | 0 / 142 (0.00%) | 0 / 145 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | | | |

| Serious adverse events | Prevnar 13/Infanrix hexa Group | | |
|---|--------------------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 142 (0.00%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | | | |

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

| Non-serious adverse events | 10PP-LD/Infanrix hexa Group | 10PP-HD/Infanrix hexa Group | Synflorix/Infanrix hexa Group |
|---|--|-----------------------------|-------------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 118 / 146 (80.82%) | 113 / 142 (79.58%) | 110 / 145 (75.86%) |
| General disorders and administration site conditions | | | |
| Pain (primary vaccination) | Additional description: Symptom reported during the 7-day post-primary vaccination periods, across doses | | |
| subjects affected / exposed ^[1] | 75 / 146 (51.37%) | 73 / 142 (51.41%) | 72 / 144 (50.00%) |
| occurrences (all) | 75 | 73 | 72 |
| Redness (primary vaccination) | Additional description: Symptom reported during the 7-day post-primary vaccination periods, across doses | | |
| subjects affected / exposed ^[2] | 96 / 146 (65.75%) | 97 / 142 (68.31%) | 88 / 144 (61.11%) |
| occurrences (all) | 96 | 97 | 88 |
| Swelling (primary vaccination) | Additional description: Symptom reported during the 7-day post-primary vaccination periods, across doses | | |
| subjects affected / exposed ^[3] | 82 / 146 (56.16%) | 74 / 142 (52.11%) | 60 / 144 (41.67%) |
| occurrences (all) | 82 | 74 | 60 |
| Drowsiness (primary vaccination) | Additional description: Symptom reported during the 7-day post-primary vaccination periods, across doses | | |
| subjects affected / exposed ^[4] | 107 / 146 (73.29%) | 96 / 142 (67.61%) | 98 / 144 (68.06%) |
| occurrences (all) | 107 | 96 | 98 |
| Irritability (primary vaccination) | Additional description: Symptom reported during the 7-day post-primary vaccination periods, across doses | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed ^[5] | 118 / 146 (80.82%) | 113 / 142 (79.58%) | 110 / 144 (76.39%) |
| occurrences (all) | 118 | 113 | 110 |
| Loss of appetite (primary vaccination) | Additional description: Symptom reported during the 7-day post-primary vaccination periods, across doses | | |
| subjects affected / exposed ^[6] | 65 / 146 (44.52%) | 59 / 142 (41.55%) | 59 / 144 (40.97%) |
| occurrences (all) | 65 | 59 | 59 |
| Fever (primary vaccination) | Additional description: (rectal temperature \geq 38°C) Symptom reported during the 7-day post-primary vaccination periods, across doses | | |

| | | | |
|---|---|-------------------------|-------------------------|
| subjects affected / exposed ^[7] occurrences (all) | 76 / 146 (52.05%) 76 | 71 / 142 (50.00%) 71 | 74 / 144 (51.39%) 74 |
| Pain (booster vaccination) | Additional description: Symptom reported during the 7-day post-booster vaccination period | | |
| subjects affected / exposed ^[8] occurrences (all) | 77 / 144 (53.47%) 77 | 73 / 140 (52.14%) 73 | 61 / 139 (43.88%) 61 |
| Redness (booster vaccination) | Additional description: Symptom reported during the 7-day post-booster vaccination period | | |
| subjects affected / exposed ^[9] occurrences (all) | 83 / 144 (57.64%) 83 | 81 / 140 (57.86%) 81 | 68 / 139 (48.92%) 68 |
| Swelling (booster vaccination) | Additional description: Symptom reported during the 7-day post-booster vaccination period | | |
| subjects affected / exposed ^[10] occurrences (all) | 70 / 144 (48.61%) 70 | 55 / 140 (39.29%) 55 | 49 / 139 (35.25%) 49 |
| Drowsiness (booster vaccination) | Additional description: Symptom reported during the 7-day post-booster vaccination period | | |
| subjects affected / exposed ^[11] occurrences (all) | 77 / 144 (53.47%) 77 | 64 / 140 (45.71%) 64 | 66 / 139 (47.48%) 66 |
| Irritability (booster vaccination) | Additional description: Symptom reported during the 7-day post-booster vaccination period | | |
| subjects affected / exposed ^[12] occurrences (all) | 95 / 144 (65.97%) 95 | 84 / 140 (60.00%) 84 | 82 / 139 (58.99%) 82 |
| Loss of appetite (booster vaccination) | Additional description: Symptom reported during the 7-day post-booster vaccination period | | |
| subjects affected / exposed ^[13] occurrences (all) | 49 / 144 (34.03%) 49 | 38 / 140 (27.14%) 38 | 36 / 139 (25.90%) 36 |
| Fever (booster vaccination) | Additional description: (rectal temperature >= 38°C) Symptom reported during the 7-day post-booster vaccination period | | |
| subjects affected / exposed ^[14] occurrences (all) | 50 / 144 (34.72%) 50 | 55 / 140 (39.29%) 55 | 51 / 139 (36.69%) 51 |
| Eye disorders | | | |
| Conjunctivitis | Additional description: Unsolicited AE reported during the 31-day post-primary vaccination periods, across doses | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 3 / 146 (2.05%) 3 | 9 / 142 (6.34%) 9 | 5 / 145 (3.45%) 5 |
| Infections and infestations | | | |
| Bronchitis | Additional description: Unsolicited AE reported during the 31-day post-primary vaccination periods, across doses | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 5 / 146 (3.42%) 5 | 11 / 142 (7.75%) 11 | 11 / 145 (7.59%) 11 |

| | | | |
|---|--|------------------|------------------|
| Nasopharyngitis (primary vaccination) | Additional description: Unsolicited AE reported during the 31-day post-primary vaccination periods, across doses | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 10 / 146 (6.85%) | 7 / 142 (4.93%) | 12 / 145 (8.28%) |
| occurrences (all) | 10 | 7 | 12 |
| Nasopharyngitis (booster vaccination) | Additional description: Unsolicited AE reported during the 31-day post-booster vaccination period | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed ^[15] | 9 / 144 (6.25%) | 4 / 140 (2.86%) | 3 / 140 (2.14%) |
| occurrences (all) | 9 | 4 | 3 |
| Rhinitis | Additional description: Unsolicited AE reported during the 31-day post-primary vaccination periods, across doses | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 11 / 146 (7.53%) | 11 / 142 (7.75%) | 12 / 145 (8.28%) |
| occurrences (all) | 11 | 11 | 12 |
| Viral infection | Additional description: Unsolicited AE reported during the 31-day post-primary vaccination periods, across doses | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 146 (0.00%) | 9 / 142 (6.34%) | 5 / 145 (3.45%) |
| occurrences (all) | 0 | 9 | 5 |

| | | | |
|---|--|--|--|
| Non-serious adverse events | Prevnar 13/Infanrix hexa Group | | |
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 113 / 142 (79.58%) | | |
| General disorders and administration site conditions | | | |
| Pain (primary vaccination) | Additional description: Symptom reported during the 7-day post-primary vaccination periods, across doses | | |
| subjects affected / exposed ^[1] | 64 / 142 (45.07%) | | |
| occurrences (all) | 64 | | |
| Redness (primary vaccination) | Additional description: Symptom reported during the 7-day post-primary vaccination periods, across doses | | |
| subjects affected / exposed ^[2] | 83 / 142 (58.45%) | | |
| occurrences (all) | 83 | | |
| Swelling (primary vaccination) | Additional description: Symptom reported during the 7-day post-primary vaccination periods, across doses | | |
| subjects affected / exposed ^[3] | 59 / 142 (41.55%) | | |
| occurrences (all) | 59 | | |
| Drowsiness (primary vaccination) | Additional description: Symptom reported during the 7-day post-primary vaccination periods, across doses | | |
| subjects affected / exposed ^[4] | 102 / 142 (71.83%) | | |
| occurrences (all) | 102 | | |

| | | | |
|--|---|--|--|
| Irritability (primary vaccination) alternative assessment type: Non-systematic subjects affected / exposed ^[5] occurrences (all) | Additional description: Symptom reported during the 7-day post-primary vaccination periods, across doses | | |
| | 113 / 142 (79.58%) | | |
| | 113 | | |
| Loss of appetite (primary vaccination) subjects affected / exposed ^[6] occurrences (all) | Additional description: Symptom reported during the 7-day post-primary vaccination periods, across doses | | |
| | 57 / 142 (40.14%) | | |
| | 57 | | |
| Fever (primary vaccination) subjects affected / exposed ^[7] occurrences (all) | Additional description: (rectal temperature $\geq 38^{\circ}\text{C}$) Symptom reported during the 7-day post-primary vaccination periods, across doses | | |
| | 65 / 142 (45.77%) | | |
| | 65 | | |
| Pain (booster vaccination) subjects affected / exposed ^[8] occurrences (all) | Additional description: Symptom reported during the 7-day post-booster vaccination period | | |
| | 68 / 140 (48.57%) | | |
| | 68 | | |
| Redness (booster vaccination) subjects affected / exposed ^[9] occurrences (all) | Additional description: Symptom reported during the 7-day post-booster vaccination period | | |
| | 66 / 140 (47.14%) | | |
| | 66 | | |
| Swelling (booster vaccination) subjects affected / exposed ^[10] occurrences (all) | Additional description: Symptom reported during the 7-day post-booster vaccination period | | |
| | 59 / 140 (42.14%) | | |
| | 59 | | |
| Drowsiness (booster vaccination) subjects affected / exposed ^[11] occurrences (all) | Additional description: Symptom reported during the 7-day post-booster vaccination period | | |
| | 73 / 140 (52.14%) | | |
| | 73 | | |
| Irritability (booster vaccination) subjects affected / exposed ^[12] occurrences (all) | Additional description: Symptom reported during the 7-day post-booster vaccination period | | |
| | 90 / 140 (64.29%) | | |
| | 90 | | |
| Loss of appetite (booster vaccination) subjects affected / exposed ^[13] occurrences (all) | Additional description: Symptom reported during the 7-day post-booster vaccination period | | |
| | 57 / 140 (40.71%) | | |
| | 57 | | |
| Fever (booster vaccination) subjects affected / exposed ^[14] occurrences (all) | Additional description: (rectal temperature $\geq 38^{\circ}\text{C}$) Symptom reported during the 7-day post-booster vaccination period | | |
| | 53 / 140 (37.86%) | | |
| | 53 | | |
| Eye disorders | | | |

| | | | |
|--|--|--|--|
| Conjunctivitis alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | Additional description: Unsolicited AE reported during the 31-day post-primary vaccination periods, across doses | | |
| | 3 / 142 (2.11%) | | |
| | 3 | | |
| Infections and infestations Bronchitis alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | Additional description: Unsolicited AE reported during the 31-day post-primary vaccination periods, across doses | | |
| | 13 / 142 (9.15%) | | |
| | 13 | | |
| Nasopharyngitis (primary vaccination) alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | Additional description: Unsolicited AE reported during the 31-day post-primary vaccination periods, across doses | | |
| | 8 / 142 (5.63%) | | |
| | 8 | | |
| Nasopharyngitis (booster vaccination) alternative assessment type: Non-systematic subjects affected / exposed ^[15] occurrences (all) | Additional description: Unsolicited AE reported during the 31-day post-booster vaccination period | | |
| | 6 / 140 (4.29%) | | |
| | 6 | | |
| Rhinitis alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | Additional description: Unsolicited AE reported during the 31-day post-primary vaccination periods, across doses | | |
| | 14 / 142 (9.86%) | | |
| | 14 | | |
| Viral infection alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | Additional description: Unsolicited AE reported during the 31-day post-primary vaccination periods, across doses | | |
| | 3 / 142 (2.11%) | | |
| | 3 | | |

Notes:

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

Justification: Solicited symptoms results are presented only for subjects for whom results were available.

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

Justification: Solicited symptoms results are presented only for subjects for whom results were available.

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

Justification: Solicited symptoms results are presented only for subjects for whom results were available.

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

Justification: Solicited symptoms results are presented only for subjects for whom results were available.

[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: Solicited symptoms results are presented only for subjects for whom results were available.

[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: Solicited symptoms results are presented only for subjects for whom results were available.

[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: Solicited symptoms results are presented only for subjects for whom results were available.

[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: Solicited symptoms results are presented only for subjects for whom results were available.

[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: Solicited symptoms results are presented only for subjects for whom results were available.

[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: Solicited symptoms results are presented only for subjects for whom results were available.

[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: Solicited symptoms results are presented only for subjects for whom results were available.

[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: Solicited symptoms results are presented only for subjects for whom results were available.

[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: Solicited symptoms results are presented only for subjects for whom results were available.

[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: Solicited symptoms results are presented only for subjects for whom results were available.

[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: Solicited symptoms results are presented only for subjects for whom results were available.

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

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

| |
|--|
| The results of analysis of the anti-Ply haemolysis activity inhibition are not presented as assay was not validated. |
|--|

Notes: