

**Clinical trial results:**

A phase IIIa single-blind, controlled multicentre study to assess the safety, reactogenicity and immunogenicity of GSK Biologicals 10-valent pneumococcal conjugate vaccine or Prevenar when given as a fourth dose between 12-18 months of age in children previously vaccinated in infancy in the primary study 10PN-PD-DIT-001 (105553) with either GSK Biologicals 10-valent pneumococcal conjugate vaccine or Prevenar.

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

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2006-001628-38 |
| Trial protocol | FI FR |
| Global end of trial date | 06 November 2007 |

Results information

| | |
|--------------------------------|--|
| Result version number | v2 |
| This version publication date | 19 March 2016 |
| First version publication date | 29 April 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 Correction of errors detected in immunogenicity data |

Trial information**Trial identification**

| | |
|-----------------------|--------|
| Sponsor protocol code | 107046 |
|-----------------------|--------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00370396 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | GlaxoSmithKline Biologicals |
| Sponsor organisation address | Rue de l'Institut 89, Rixensart, Belgium, B-1330 |
| Public contact | Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089904466, GSKClinicalSupportHD@gsk.com |
| Scientific contact | Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 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 | Yes |

| | |
|--------------------------------|--|
| 1901/2006 apply to this trial? | |
|--------------------------------|--|

Notes:

Results analysis stage

| | |
|--|--------------|
| Analysis stage | Final |
| Date of interim/final analysis | 13 June 2008 |
| Is this the analysis of the primary completion data? | No |

| | |
|----------------------------------|------------------|
| Global end of trial reached? | Yes |
| Global end of trial date | 06 November 2007 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To demonstrate that a booster dose of GSK Biologicals' 10-valent pneumococcal conjugate vaccine is non-inferior to Prevenar, both co-administered with DTPa-HBV-IPV/Hib vaccine, in terms of post-immunization febrile reactions with rectal fever > 39.0°C.

Criteria for safety:

Non-inferiority will be demonstrated if the upper limit of the 95% CI of the difference (10Pn-10Pn group minus 7Pn-7Pn group), in terms of percentage of subjects with rectal fever >39.0°C, is lower than 10%.

Protection of trial subjects:

All subjects were supervised after vaccination/product administration with appropriate medical treatment readily available. Vaccines/products were administered by qualified and trained personnel. Vaccines/products were administered only to eligible subjects that had no contraindications to any components of the vaccines/products. Towards ensuring the safety of subjects, the study design included an Active Primary Phase (Months 0-1) followed by an additional 5-months Extended Safety Follow-up Phase (ESFU (up to 6 months after the last vaccination/product administration during an). Prior to vaccination, subjects' pre-vaccination body temperature was also evaluated.

Background therapy: -

Evidence for comparator: -

| | |
|---|-------------------|
| Actual start date of recruitment | 25 September 2006 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Safety |
| Long term follow-up duration | 5 Months |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|--------------|
| Country: Number of subjects enrolled | Finland: 398 |
| Country: Number of subjects enrolled | France: 142 |
| Country: Number of subjects enrolled | Poland: 572 |
| Worldwide total number of subjects | 1112 |
| EEA total number of subjects | 1112 |

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) | 1112 |
| 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:

This study consisted of approximately 1200 subjects who were previously enrolled and had been vaccinated with either the 10Pn or 7Pn vaccine as part of the 10PN-PD-DIT-001 (105553) study (EudraCTnumber: 2005-003300-11).

Pre-assignment

Screening details:

During the screening the following was performed: informed consent was obtained and signed from parents or guardians of subjects, check for inclusion/exclusion criteria and contraindications/precautions was performed, and medical history of subjects was collected. Prior to vaccination, subjects' pre-vaccination body temperature was evaluated.

Period 1

| | |
|------------------------------|---------------------------------------|
| Period 1 title | Overall Study Period (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Single blind |
| Roles blinded | Subject |

Arms

| | |
|------------------------------|-----------------|
| Are arms mutually exclusive? | Yes |
| Arm title | 10Pn-10Pn Group |

Arm description:

This group consisted of subjects previously vaccinated with the 10Pn-PD-DiT vaccine (also referred as 10Pn vaccine or Synflorix™) as part of a previous study by GSK Biologicals – the 10PN-PD-DIT-001 (105553) study (EuDRA-CT number: 2005-003300-11). As part of the 105553 study, subjects had received a 3-dose primary vaccination of 10Pn vaccine at 2, 3 and 4 months of age (injected intramuscularly [IM] in the right thigh) co-administered with DTPa-HBV-IPV/Hib vaccine (or Infanrix hexa™), except for the second dose in France, which was co-administered with DTPa-IPV/Hib (or Infanrix™ IPV Hib), injected intramuscularly in the left thigh. As part of this study, at 12-18 months of age, subjects received a booster dose of 10Pn vaccine, injected IM in the right thigh or deltoid, co-administered with DTPa-HBV-IPV/Hib vaccine, injected IM in the left thigh or deltoid.

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

Dosage and administration details:

One dose administered at 12-18 months of age in the left thigh or deltoid

| | |
|--|---|
| Investigational medicinal product name | DTPa-HBV-IPV/Hib |
| Investigational medicinal product code | |
| Other name | Infanrix hexa™ (by GSK Biologicals) |
| Pharmaceutical forms | Powder and solvent for suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

One dose administered at at 12-18 months of age in the right thigh or deltoid

| | |
|------------------|---------------|
| Arm title | 7Pn-7Pn Group |
|------------------|---------------|

Arm description:

This group consisted of subjects previously vaccinated with the 7Pn vaccine (also referred as Prevenar™) as part of a previous study by GSK Biologicals – the 10PN-PD-DIT-001 (105553) study (EuDRA-CT number: 2005-003300-11). As part of the 105553 study, subjects had received a 3-dose primary vaccination of 7Pn vaccine at 2, 3 and 4 months of age (injected intramuscularly [IM] in the

right thigh) co-administered with DTPa-HBV-IPV/Hib vaccine (or Infanrix hexa™), except for the second dose in France, which was co-administered with DTPa-IPV/Hib (or Infanrix™ IPV Hib), injected intramuscularly in the left thigh. As part of this study, at 12-18 months of age, subjects received a booster dose of 7Pn vaccine, injected IM in the right thigh or deltoid, co-administered with DTPa-HBV-IPV/Hib vaccine, injected IM in the left thigh or deltoid.

| | |
|--|--|
| Arm type | Active comparator |
| Investigational medicinal product name | 7Pn |
| Investigational medicinal product code | |
| Other name | Prevenar™ by Wyeth Lederle Vaccines S.A. |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

One dose administered at 12-18 months of age in the left thigh or deltoid

| | |
|--|---|
| Investigational medicinal product name | DTPa-HBV-IPV/Hib |
| Investigational medicinal product code | |
| Other name | Infanrix hexa™ (by GSK Biologicals) |
| Pharmaceutical forms | Powder and solvent for suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

One dose administered at at 12-18 months of age in the right thigh or deltoid

| | |
|------------------|----------------|
| Arm title | 7Pn-10Pn Group |
|------------------|----------------|

Arm description:

This group consisted of subjects previously vaccinated with the 7Pn vaccine (also referred as Prevenar™) as part of a previous study by GSK Biologicals – the 10PN-PD-DIT-001 (105553) study (EuDRA-CT number: 2005-003300-11). As part of the 105553 study, subjects had received a 3-dose primary vaccination of 7Pn vaccine at 2, 3 and 4 months of age (injected intramuscularly [IM] in the right thigh) co-administered with DTPa-HBV-IPV/Hib vaccine (or Infanrix hexa™), except for the second dose in France, which was co-administered with DTPa-IPV/Hib (or Infanrix™ IPV Hib), injected intramuscularly in the left thigh. As part of this study, at 12-18 months of age, subjects received a booster dose of 10Pn-PD-DiT vaccine (also referred as 10Pn vaccine or Synflorix™), injected IM in the right thigh or deltoid, co-administered with DTPa-HBV-IPV/Hib vaccine, injected IM in the left thigh or deltoid.

| | |
|--|--|
| Arm type | Active comparator |
| Investigational medicinal product name | 10 valent streptococcus pneumoniae conjugate vaccine |
| Investigational medicinal product code | |
| Other name | 10Pn-PD-DiT, Synflorix™ (by GSK Biologicals) |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

One dose administered at 12-18 months of age in the left thigh or deltoid

| | |
|--|---|
| Investigational medicinal product name | DTPa-HBV-IPV/Hib |
| Investigational medicinal product code | |
| Other name | Infanrix hexa™ (by GSK Biologicals) |
| Pharmaceutical forms | Powder and solvent for suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

One dose administered at at 12-18 months of age in the right thigh or deltoid

| Number of subjects in period 1 | 10Pn-10Pn Group | 7Pn-7Pn Group | 7Pn-10Pn Group |
|---------------------------------------|-----------------|---------------|----------------|
| Started | 737 | 92 | 283 |
| Overall Study Period | 737 | 92 | 283 |
| Completed | 726 | 91 | 282 |
| Not completed | 11 | 1 | 1 |
| Consent withdrawn by subject | - | - | 1 |
| Lost to follow-up | 11 | 1 | - |

Baseline characteristics

Reporting groups

| | |
|-----------------------|-----------------|
| Reporting group title | 10Pn-10Pn Group |
|-----------------------|-----------------|

Reporting group description:

This group consisted of subjects previously vaccinated with the 10Pn-PD-DiT vaccine (also referred as 10Pn vaccine or Synflorix™) as part of a previous study by GSK Biologicals – the 10PN-PD-DIT-001 (105553) study (EuDRA-CT number: 2005-003300-11). As part of the 105553 study, subjects had received a 3-dose primary vaccination of 10Pn vaccine at 2, 3 and 4 months of age (injected intramuscularly [IM] in the right thigh) co-administered with DTPa-HBV-IPV/Hib vaccine (or Infanrix hexa™), except for the second dose in France, which was co-administered with DTPa-IPV/Hib (or Infanrix™ IPV Hib), injected intramuscularly in the left thigh. As part of this study, at 12-18 months of age, subjects received a booster dose of 10Pn vaccine, injected IM in the right thigh or deltoid, co-administered with DTPa-HBV-IPV/Hib vaccine, injected IM in the left thigh or deltoid.

| | |
|-----------------------|---------------|
| Reporting group title | 7Pn-7Pn Group |
|-----------------------|---------------|

Reporting group description:

This group consisted of subjects previously vaccinated with the 7Pn vaccine (also referred as Prevenar™) as part of a previous study by GSK Biologicals – the 10PN-PD-DIT-001 (105553) study (EuDRA-CT number: 2005-003300-11). As part of the 105553 study, subjects had received a 3-dose primary vaccination of 7Pn vaccine at 2, 3 and 4 months of age (injected intramuscularly [IM] in the right thigh) co-administered with DTPa-HBV-IPV/Hib vaccine (or Infanrix hexa™), except for the second dose in France, which was co-administered with DTPa-IPV/Hib (or Infanrix™ IPV Hib), injected intramuscularly in the left thigh. As part of this study, at 12-18 months of age, subjects received a booster dose of 7Pn vaccine, injected IM in the right thigh or deltoid, co-administered with DTPa-HBV-IPV/Hib vaccine, injected IM in the left thigh or deltoid.

| | |
|-----------------------|----------------|
| Reporting group title | 7Pn-10Pn Group |
|-----------------------|----------------|

Reporting group description:

This group consisted of subjects previously vaccinated with the 7Pn vaccine (also referred as Prevenar™) as part of a previous study by GSK Biologicals – the 10PN-PD-DIT-001 (105553) study (EuDRA-CT number: 2005-003300-11). As part of the 105553 study, subjects had received a 3-dose primary vaccination of 7Pn vaccine at 2, 3 and 4 months of age (injected intramuscularly [IM] in the right thigh) co-administered with DTPa-HBV-IPV/Hib vaccine (or Infanrix hexa™), except for the second dose in France, which was co-administered with DTPa-IPV/Hib (or Infanrix™ IPV Hib), injected intramuscularly in the left thigh. As part of this study, at 12-18 months of age, subjects received a booster dose of 10Pn-PD-DiT vaccine (also referred as 10Pn vaccine or Synflorix™), injected IM in the right thigh or deltoid, co-administered with DTPa-HBV-IPV/Hib vaccine, injected IM in the left thigh or deltoid.

| Reporting group values | 10Pn-10Pn Group | 7Pn-7Pn Group | 7Pn-10Pn Group |
|---|-----------------|---------------|----------------|
| Number of subjects | 737 | 92 | 283 |
| 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: months geometric mean | 15.3 | 14.2 | 14.2 |

| | | | |
|--------------------|--------|--------|--------|
| standard deviation | ± 2.08 | ± 2.26 | ± 2.23 |
|--------------------|--------|--------|--------|

| | | | |
|---------------------------------------|-----|----|-----|
| Gender categorical Units: Subjects | | | |
| Female | 360 | 50 | 134 |
| Male | 377 | 42 | 149 |

| | | | |
|---|-------|--|--|
| Reporting group values | Total | | |
| Number of subjects | 1112 | | |
| 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: months geometric mean standard deviation | - | | |
| Gender categorical Units: Subjects | | | |
| Female | 544 | | |
| Male | 568 | | |

End points

End points reporting groups

| | |
|-----------------------|-----------------|
| Reporting group title | 10Pn-10Pn Group |
|-----------------------|-----------------|

Reporting group description:

This group consisted of subjects previously vaccinated with the 10Pn-PD-DiT vaccine (also referred as 10Pn vaccine or Synflorix™) as part of a previous study by GSK Biologicals – the 10PN-PD-DIT-001 (105553) study (EuDRA-CT number: 2005-003300-11). As part of the 105553 study, subjects had received a 3-dose primary vaccination of 10Pn vaccine at 2, 3 and 4 months of age (injected intramuscularly [IM] in the right thigh) co-administered with DTPa-HBV-IPV/Hib vaccine (or Infanrix hexa™), except for the second dose in France, which was co-administered with DTPa-IPV/Hib (or Infanrix™ IPV Hib), injected intramuscularly in the left thigh. As part of this study, at 12-18 months of age, subjects received a booster dose of 10Pn vaccine, injected IM in the right thigh or deltoid, co-administered with DTPa-HBV-IPV/Hib vaccine, injected IM in the left thigh or deltoid.

| | |
|-----------------------|---------------|
| Reporting group title | 7Pn-7Pn Group |
|-----------------------|---------------|

Reporting group description:

This group consisted of subjects previously vaccinated with the 7Pn vaccine (also referred as Prevenar™) as part of a previous study by GSK Biologicals – the 10PN-PD-DIT-001 (105553) study (EuDRA-CT number: 2005-003300-11). As part of the 105553 study, subjects had received a 3-dose primary vaccination of 7Pn vaccine at 2, 3 and 4 months of age (injected intramuscularly [IM] in the right thigh) co-administered with DTPa-HBV-IPV/Hib vaccine (or Infanrix hexa™), except for the second dose in France, which was co-administered with DTPa-IPV/Hib (or Infanrix™ IPV Hib), injected intramuscularly in the left thigh. As part of this study, at 12-18 months of age, subjects received a booster dose of 7Pn vaccine, injected IM in the right thigh or deltoid, co-administered with DTPa-HBV-IPV/Hib vaccine, injected IM in the left thigh or deltoid.

| | |
|-----------------------|----------------|
| Reporting group title | 7Pn-10Pn Group |
|-----------------------|----------------|

Reporting group description:

This group consisted of subjects previously vaccinated with the 7Pn vaccine (also referred as Prevenar™) as part of a previous study by GSK Biologicals – the 10PN-PD-DIT-001 (105553) study (EuDRA-CT number: 2005-003300-11). As part of the 105553 study, subjects had received a 3-dose primary vaccination of 7Pn vaccine at 2, 3 and 4 months of age (injected intramuscularly [IM] in the right thigh) co-administered with DTPa-HBV-IPV/Hib vaccine (or Infanrix hexa™), except for the second dose in France, which was co-administered with DTPa-IPV/Hib (or Infanrix™ IPV Hib), injected intramuscularly in the left thigh. As part of this study, at 12-18 months of age, subjects received a booster dose of 10Pn-PD-DiT vaccine (also referred as 10Pn vaccine or Synflorix™), injected IM in the right thigh or deltoid, co-administered with DTPa-HBV-IPV/Hib vaccine, injected IM in the left thigh or deltoid.

Primary: Number of subjects with rectal temperature above (>) 39.0 degrees Celsius (°C) post booster between the 10Pn-10Pn and 7Pn-7Pn groups

| | |
|-----------------|---|
| End point title | Number of subjects with rectal temperature above (>) 39.0 degrees Celsius (°C) post booster between the 10Pn-10Pn and 7Pn-7Pn groups ^[1] |
|-----------------|---|

End point description:

Fever was measured as rectal temperature. Assessment of occurrences of rectal temperature > 39.0 °C was performed post administration of the booster dose of pneumococcal vaccine (10PN or 7Pn vaccine) in this study. The analysis was performed on the Total vaccinated cohort, which included all subjects vaccinated in this study 10PN-PD-DIT-007, solely on subjects with results available.

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

End point timeframe:

Within 4 days (Days 0-3) after the booster vaccination at Month 0 in this study 10PN-PD-DIT-007

Notes:

[1] - 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 was not assessed in the 7Pn-10Pn Group.

| End point values | 10Pn-10Pn Group | 7Pn-7Pn Group | | |
|--|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 735 | 91 | | |
| Units: Subjects | | | | |
| Subjects with rectal temperature >39°C | 24 | 7 | | |

Statistical analyses

| Statistical analysis title | Non-inferiority of 10Pn vs 7Pn vaccine |
|----------------------------|--|
|----------------------------|--|

Statistical analysis description:

Analysis aimed at demonstrating the non-inferiority of 10Pn vs 7Pn vaccine, both co-administered with DTPa-HBV-IPV/Hib vaccine, in terms of post-immunization febrile reactions with rectal fever > 39.0°C. Towards this, standardized asymptotic 95% confidence interval (CI) for the difference [10Pn-10Pn minus 7Pn-7Pn] in terms of percentages of subjects reporting rectal fever >39.0°C was computed.

| | |
|---|---------------------------------|
| Comparison groups | 7Pn-7Pn Group v 10Pn-10Pn Group |
| Number of subjects included in analysis | 826 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[2] |
| Parameter estimate | Difference in percentage |
| Point estimate | -4.43 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -11.85 |
| upper limit | -0.21 |

Notes:

[2] - Non-inferiority was demonstrated if the upper limit of the computed standardized asymptotic 95% CI was lower than the pre-defined limit of 10%.

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

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

End point description:

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. The analysis was performed on the Total vaccinated cohort, which included all subjects vaccinated in this study 10PN-PD-DIT-007, solely on subjects with results available.

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

End point timeframe:

Within 4 days (Days 0-3) after the booster vaccination at Month 0 in this study 10PN-PD-DIT-007

| End point values | 10Pn-10Pn Group | 7Pn-7Pn Group | 7Pn-10Pn Group | |
|-----------------------------|-----------------|-----------------|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 735 | 91 | 282 | |
| Units: Subjects | | | | |
| Any Pain | 452 | 48 | 150 | |
| Grade 3 Pain | 47 | 3 | 18 | |

| | | | | |
|------------------|-----|----|-----|--|
| Any Swelling | 338 | 42 | 112 | |
| Grade 3 Swelling | 67 | 7 | 20 | |
| Any Redness | 451 | 59 | 153 | |
| Grade 3 Redness | 96 | 7 | 19 | |

Statistical analyses

No statistical analyses for this end point

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

| | |
|-----------------|--|
| End point title | Number of subjects with any and any Grade 3 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. 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 everyday activities. Grade 3 loss of appetite was defined as the subject not eating at all. "Any" is defined as incidence of the specified symptom regardless of intensity or relationship to study vaccination. The analysis was performed on the Total vaccinated cohort, which included all subjects vaccinated in this study 10PN-PD-DIT-007, solely on subjects with results available.

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

End point timeframe:

Within 4 days (Days 0-3) after the booster vaccination at Month 0 in this study 10PN-PD-DIT-007

| End point values | 10Pn-10Pn Group | 7Pn-7Pn Group | 7Pn-10Pn Group | |
|-----------------------------|-----------------|-----------------|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 735 | 91 | 282 | |
| Units: Subjects | | | | |
| Any drowsiness | 303 | 48 | 130 | |
| Grade 3 drowsiness | 5 | 0 | 5 | |
| Any fever | 245 | 33 | 112 | |
| Grade 3 fever | 1 | 2 | 3 | |
| Any irritability | 438 | 55 | 176 | |
| Grade 3 irritability | 15 | 2 | 12 | |
| Any loss of appetite | 230 | 31 | 92 | |
| Grade 3 loss of appetite | 4 | 0 | 3 | |

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" is defined as an incidence of an unsolicited AE regardless of intensity or relationship to study vaccination. The analysis was performed on the Total vaccinated cohort, which included all subjects vaccinated in this study 10PN-PD-DIT-007.

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

End point timeframe:

Within 31 days (Day 0-30) after the booster vaccination at Month 0 in this study 10PN-PD-DIT-007

| End point values | 10Pn-10Pn Group | 7Pn-7Pn Group | 7Pn-10Pn Group | |
|-----------------------------------|-----------------|-----------------|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 737 | 92 | 283 | |
| Units: Subjects | | | | |
| Subject(s) with unsolicited AE(s) | 188 | 32 | 99 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with serious adverse events (SAEs) during the Active Phase of the study

| | |
|-----------------|--|
| End point title | Number of subjects with serious adverse events (SAEs) during the Active Phase of the study |
|-----------------|--|

End point description:

An SAE is any untoward medical occurrence that: results in death, is life-threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, or may evolve into one of the outcomes listed above. "Any" is defined as an incidence of a SAE regardless of intensity/severity. The analysis was performed on the Total vaccinated cohort, which included all subjects vaccinated in this study 10PN-PD-DIT-007.

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

End point timeframe:

Throughout the Active Phase of the study, that is, within 31 days (Day 0-30) after the booster vaccination at Month 0 in this study 10PN-PD-DIT-007

| End point values | 10Pn-10Pn Group | 7Pn-7Pn Group | 7Pn-10Pn Group | |
|-----------------------------|-----------------|-----------------|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 737 | 92 | 283 | |
| Units: Subjects | | | | |
| Subject(s) with SAEs | 12 | 1 | 4 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with serious adverse events (SAEs) during the entire study

| | |
|-----------------|---|
| End point title | Number of subjects with serious adverse events (SAEs) during the entire study |
|-----------------|---|

End point description:

An SAE is any untoward medical occurrence that: results in death, is life-threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, or may evolve into one of the outcomes listed above. "Any" is defined as an incidence of a SAE regardless of intensity/severity. The analysis was performed on the Total vaccinated cohort, which included all subjects vaccinated in this study 10PN-PD-DIT-007, solely on subjects enrolled in the ESFU Phase of the study.

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

End point timeframe:

Throughout the study period, from Month 0 prior to booster vaccination up to Month 6, end of the ESFU in this study 10PN-PD-DIT-007

| End point values | 10Pn-10Pn Group | 7Pn-7Pn Group | 7Pn-10Pn Group | |
|-----------------------------|-----------------|-----------------|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 726 | 92 | 282 | |
| Units: Subjects | | | | |
| Subject(s) with SAEs | 33 | 6 | 8 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seroprotected as regards anti-pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F antigens – by 22F-inhibition Enzyme-linked immunosorbent assay (ELISA)

| | |
|-----------------|--|
| End point title | Number of subjects seroprotected as regards anti-pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F antigens – by 22F-inhibition Enzyme-linked immunosorbent assay (ELISA) |
|-----------------|--|

End point description:

A seroprotected subject as regards anti-pneumococcal serotype antibody was defined as a subject with anti-pneumococcal serotype antibody concentration above than or equal to (\geq) 0.20 microgram per millilitre ($\mu\text{g/mL}$). Anti-pneumococcal serotypes antibodies assessed were antibodies against pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F (Anti-1, -4, -5, -6B, -7F, 9V, -14, -18C, -19F and -23F). Analysis was performed using the 22F-inhibition Enzyme-linked immunosorbent assay (ELISA), using $\geq 0.05 \mu\text{g/mL}$ as seropositivity cut off. For this endpoint, the analysis was performed on the according-to-protocol cohort for immunogenicity, e. a., evaluable subjects for whom assay results were available for antibodies against at least one study vaccine antigen component after booster vaccination.

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

End point timeframe:

Prior to (PRE) and one month after (Month 1) booster vaccination

| End point values | 10Pn-10Pn Group | 7Pn-7Pn Group | 7Pn-10Pn Group | |
|----------------------------------|-----------------|-----------------|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 347 | 89 | 134 | |
| Units: Subjects | | | | |
| Anti-1 PRE (N=338;82;133) | 123 | 3 | 3 | |
| Anti-1 Month 1 (N=342;81;133) | 340 | 4 | 113 | |
| Anti-4 PRE (N=342;78;131) | 196 | 53 | 99 | |
| Anti-4 Month 1 (N=343;88;133) | 342 | 88 | 133 | |
| Anti-5 PRE (N=344;84;134) | 231 | 5 | 14 | |
| Anti-5 Month 1 (N=342;82;133) | 340 | 5 | 114 | |
| Anti-6B PRE (N=333;75;131) | 223 | 23 | 69 | |
| Anti-6B Month 1 (N=341 ;87;133) | 329 | 85 | 131 | |
| Anti-7F PRE (N=340;85;133) | 308 | 4 | 3 | |
| Anti-7F Month 1 (N=342;85;133) | 342 | 6 | 127 | |
| Anti-9V PRE (N=344;77;130) | 291 | 70 | 123 | |
| Anti-9V Month 1 (N=340;89;133) | 340 | 89 | 133 | |
| Anti-14 PRE (N=336;75;130) | 268 | 70 | 125 | |
| Anti-14 Month 1 (N=339;86;133) | 336 | 86 | 133 | |
| Anti-18C PRE (N=341;83;131) | 240 | 60 | 107 | |
| Anti-18C Month 1 (N=343;87;134) | 343 | 87 | 133 | |
| Anti-19F PRE (N=347;85;134) | 272 | 38 | 76 | |
| Anti-19F Month 1 (N=343;87;134) | 341 | 87 | 131 | |
| Anti-23F PRE (N=338;77;130) | 206 | 43 | 98 | |
| Anti-23F Month 1 (N=341;88;132) | 332 | 87 | 128 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations against pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F (Anti-1, -4, -5, -6B, -7F, 9V, -14, -18C, -19F and -23F) – by 22F-inhibition Enzyme-linked immunosorbent assay (ELISA)

| | |
|-----------------|---|
| End point title | Antibody concentrations against pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F (Anti-1, -4, -5, -6B, -7F, 9V, -14, -18C, -19F and -23F) – by 22F-inhibition Enzyme-linked immunosorbent assay (ELISA) |
|-----------------|---|

End point description:

Anti-pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F antibody concentrations (Anti-1, -4, -5, -6B, -7F, -9V, -14, -18C, -19F and -23F) were calculated, expressed as geometric mean concentrations (GMCs), in microgram per millilitre (µg/mL). The seropositivity cut-off for the assay was ≥ 0.05 µg/mL. Antibody concentrations below the cut-off of the assay were given an arbitrary value of half the cut-off for the purpose of GMC calculation. For this endpoint, the analysis was performed on the according-to-protocol cohort for immunogenicity, e. a., evaluable subjects for whom assay results were available for antibodies against at least one study vaccine antigen component after booster vaccination.

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

End point timeframe:

Prior to (PRE) and one month (Month 1) post booster vaccination

| End point values | 10Pn-10Pn Group | 7Pn-7Pn Group | 7Pn-10Pn Group | |
|--|---------------------|----------------------|---------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 347 | 89 | 134 | |
| Units: µg/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-1 PRE (N=338;82;133) | 0.14 (0.13 to 0.16) | 0.03 (0.03 to 0.04) | 0.03 (0.03 to 0.04) | |
| Anti-1 Month 1 (N=342;81;133) | 1.53 (1.4 to 1.68) | 0.04 (0.03 to 0.05) | 0.67 (0.56 to 0.8) | |
| Anti-4 PRE (N=342;78;131) | 0.23 (0.21 to 0.26) | 0.3 (0.25 to 0.37) | 0.35 (0.3 to 0.41) | |
| Anti-4 Month 1 (N=343;88;133) | 3.35 (3.06 to 3.67) | 4.4 (3.75 to 5.15) | 4.47 (3.85 to 5.19) | |
| Anti-5 PRE (N=344;84;134) | 0.27 (0.25 to 0.3) | 0.04 (0.04 to 0.05) | 0.05 (0.04 to 0.05) | |
| Anti-5 Month 1 (N=342;82;133) | 2.2 (2 to 2.42) | 0.05 (0.04 to 0.07) | 0.74 (0.6 to 0.9) | |
| Anti-6B PRE (N=333;75;131) | 0.31 (0.27 to 0.35) | 0.14 (0.11 to 0.19) | 0.26 (0.2 to 0.33) | |
| Anti-6B Month 1 (N=341 ;87;133) | 1.94 (1.74 to 2.17) | 3.53 (2.83 to 4.41) | 1.74 (1.48 to 2.05) | |
| Anti-7F PRE (N=340;85;133) | 0.57 (0.52 to 0.62) | 0.03 (0.03 to 0.04) | 0.03 (0.03 to 0.03) | |
| Anti-7F Month 1 (N=342;85;133) | 3.5 (3.25 to 3.76) | 0.04 (0.03 to 0.05) | 1.83 (1.49 to 2.24) | |
| Anti-9V PRE (N=344;77;130) | 0.54 (0.48 to 0.6) | 0.62 (0.51 to 0.76) | 0.78 (0.68 to 0.89) | |
| Anti-9V Month 1 (N=340;89;133) | 3.25 (2.99 to 3.53) | 6.09 (5.19 to 7.15) | 1.94 (1.73 to 2.19) | |
| Anti-14 PRE (N=336;75;130) | 0.66 (0.56 to 0.76) | 1.06 (0.82 to 1.38) | 1.69 (1.4 to 2.03) | |
| Anti-14 Month 1 (N=339;86;133) | 5.56 (5.01 to 6.18) | 9.29 (7.85 to 10.99) | 4.76 (4.12 to 5.49) | |
| Anti-18C PRE (N=341;83;131) | 0.3 (0.28 to 0.34) | 0.32 (0.26 to 0.39) | 0.37 (0.32 to 0.43) | |
| Anti-18C Month 1 (N=343;87;134) | 5.01 (4.6 to 5.46) | 5.21 (4.44 to 6.11) | 4.98 (4.17 to 5.93) | |
| Anti-19F PRE (N=347;85 ;134) | 0.53 (0.46 to 0.61) | 0.23 (0.17 to 0.31) | 0.31 (0.24 to 0.41) | |
| Anti-19F Month 1 (N=343;87;134) | 6.05 (5.46 to 6.71) | 3.35 (2.83 to 3.97) | 5.06 (4.24 to 6.04) | |
| Anti-23F PRE (N=338;77;130) | 0.27 (0.23 to 0.31) | 0.24 (0.19 to 0.31) | 0.4 (0.32 to 0.5) | |
| Anti-23F Month 1 (N=341;88;132) | 2.38 (2.13 to 2.66) | 6.67 (5.38 to 8.26) | 2.42 (1.99 to 2.95) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Opsonophagocytic activity (OPA) titers against pneumococcal serotypes

1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F

| | |
|-----------------|---|
| End point title | Opsonophagocytic activity (OPA) titers against pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F |
|-----------------|---|

End point description:

OPA titers against pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F (Opsono-1, -4, -5, -6B, -7F, -9V, -14, -18C, -19F and -23F) were calculated, expressed as geometric mean titers (GMTs) and tabulated. The seropositivity cut-off for the assay was ≥ 8 . Antibody titers below the cut-off of the assay were given an arbitrary value of half the cut-off for the purpose of GMT calculation. For this endpoint, the analysis was performed on the according-to-protocol cohort for immunogenicity, e. a., evaluable subjects for whom assay results were available for antibodies against at least one study vaccine antigen component after booster vaccination.

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

End point timeframe:

Prior to (PRE) and one month (Month 1) post booster vaccination

| End point values | 10Pn-10Pn Group | 7Pn-7Pn Group | 7Pn-10Pn Group | |
|--|---------------------------|---------------------------|---------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 326 | 83 | 126 | |
| Units: Titer | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Opsono-1 PRE (N=326;83;126) | 6.1 (5.4 to 6.9) | 5 (4.1 to 6) | 4.9 (4.2 to 5.8) | |
| Opsono-1 Month 1 (N=301;83;121) | 192.2 (157.5 to 234.6) | 4.3 (3.9 to 4.7) | 8.3 (6.7 to 10.4) | |
| Opsono-4 PRE (N=295;79;112) | 20.3 (16.2 to 25.5) | 24.5 (15.4 to 38.8) | 37.8 (24.8 to 57.7) | |
| Opsono-4 Month 1 (N=297;81;123) | 1856.3 (1666.1 to 2068) | 2812.6 (2282.5 to 3465.9) | 1528.9 (1286.5 to 1817) | |
| Opsono-5 PRE (N=305;79;124) | 8.2 (7.2 to 9.4) | 4.4 (3.9 to 4.9) | 4.1 (3.9 to 4.3) | |
| Opsono-5 Month 1 (N=299;83;122) | 144.1 (122.1 to 170) | 4.1 (3.9 to 4.4) | 9.5 (7.5 to 11.9) | |
| Opsono-6B PRE (N=284;75;120) | 60.3 (44.6 to 81.7) | 51.4 (27.1 to 97.5) | 36.7 (23.3 to 57.7) | |
| Opsono-6B Month 1 (N=295;79;118) | 981.2 (830.7 to 1159.1) | 3459.6 (2535.7 to 4720.3) | 640.2 (480.7 to 852.7) | |
| Opsono-7F PRE (N=294;76;117) | 377.7 (279.8 to 509.9) | 34.8 (17.5 to 69.3) | 25.3 (15.4 to 41.6) | |
| Opsono-7F Month 1 (N=296;74;118) | 4330.3 (3836 to 4888.3) | 25.2 (13.1 to 48.7) | 2397.2 (1929.2 to 2978.7) | |
| Opsono-9V PRE (N=309;81;122) | 296.9 (259.3 to 339.9) | 305.5 (227.1 to 411) | 305.1 (248.7 to 374.4) | |
| Opsono-9V Month 1 (N=297;79;120) | 2343.5 (2097.1 to 2618.7) | 5357.4 (4212.5 to 6813.6) | 886.8 (747.7 to 1051.8) | |
| Opsono-14 PRE (N=299;79;118) | 188.1 (149.9 to 235.9) | 201.6 (129.4 to 314.2) | 391.1 (303.1 to 504.6) | |
| Opsono-14 Month 1 (N=304;82;123) | 2085.9 (1868 to 2329.1) | 2134.2 (1689.1 to 2696.6) | 977.8 (828.9 to 1153.5) | |
| Opsono-18C PRE (N=309;82;121) | 8.7 (7.4 to 10.3) | 10.4 (7.4 to 14.7) | 8.5 (6.6 to 10.9) | |
| Opsono-18C Month 1 (N=299;76;121) | 810.3 (712.4 to 921.7) | 968.7 (724.1 to 1295.8) | 610.7 (480.3 to 776.4) | |

| | | | | |
|-----------------------------------|---------------------------|------------------------------|---------------------------|--|
| Opsono-19F PRE (N=317;81;123) | 10.5 (8.9 to 12.3) | 5.9 (4.5 to 7.8) | 7.3 (5.5 to 9.6) | |
| Opsono-19F Month 1 (N=293;80;120) | 624.3 (509.7 to 764.7) | 287.8 (190.8 to 434.3) | 530.1 (393 to 715.2) | |
| Opsono-23F PRE (N=305;77;120) | 171.5 (126.3 to 232.8) | 205.8 (110.1 to 384.6) | 532.9 (344.4 to 824.7) | |
| Opsono-23F Month 1 (N=301;80;122) | 2830.1 (2487.2 to 3220.3) | 13900.7 (10177.4 to 18986.1) | 2828.8 (2234.3 to 3581.6) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations to protein D (Anti-PD) - by Enzyme-Linked Immunosorbent Assay (ELISA)

| | |
|-----------------|---|
| End point title | Antibody concentrations to protein D (Anti-PD) - by Enzyme-Linked Immunosorbent Assay (ELISA) |
|-----------------|---|

End point description:

Anti-protein D (Anti-PD) antibody concentrations by Enzyme-Linked Immunosorbent Assay (ELISA) were calculated, expressed as geometric mean concentrations (GMCs) in ELISA unit per milli-liter (EL.U/mL) and tabulated. The seropositivity cut-off for the assay was ≥ 100 EL.U/mL. Antibody concentrations below the cut-off of the assay were given an arbitrary value of half the cut-off for the purpose of GMC calculation. For this endpoint, the analysis was performed on the according-to-protocol cohort for immunogenicity, e. a., evaluable subjects for whom assay results were available for antibodies against at least one study vaccine antigen component after booster vaccination.

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

End point timeframe:

Prior to (PRE) and one month (Month 1) post booster vaccination

| End point values | 10Pn-10Pn Group | 7Pn-7Pn Group | 7Pn-10Pn Group | |
|--|---------------------------|-------------------|------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 340 | 86 | 134 | |
| Units: EL.U/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-PD, PRE (N=338;73;127) | 556.4 (494.7 to 625.7) | 72.3 (59.3 to 88) | 78.1 (67.8 to 89.9) | |
| Anti-PD, Month 1 (N=340;86;134) | 2887.6 (2573.7 to 3239.8) | 75.3 (60 to 94.4) | 125.5 (103.4 to 152.4) | |

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 |
|-----------------|--|

End point description:

Anti-PRP antibody concentrations were calculated, expressed as geometric mean concentrations (GMCs), in microgram per milliliter ($\mu\text{g/mL}$), and tabulated. The seroprotection cut-off for the assay for the purpose of this endpoint was $\geq 0.15 \mu\text{g/mL}$. Antibody concentrations below the cut-off of the assay were given an arbitrary value of half the cut-off for the purpose of GMC calculation. For this endpoint, the analysis was performed on the according-to-protocol cohort for immunogenicity, e. a., evaluable subjects for whom assay results were available for antibodies against at least one study vaccine antigen component after booster vaccination.

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

End point timeframe:

Prior to (PRE) and one month (Month 1) post booster vaccination

| End point values | 10Pn-10Pn Group | 7Pn-7Pn Group | 7Pn-10Pn Group | |
|--|---------------------------|--------------------------|---------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 344 | 46 | 136 | |
| Units: $\mu\text{g/mL}$ | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-PRP, PRE (N=344;39;136) | 0.308 (0.272 to 0.348) | 0.231 (0.151 to 0.353) | 0.246 (0.2 to 0.304) | |
| Anti-PRP, Month 1 (N=343;46;136) | 36.634 (31.897 to 42.074) | 25.731 (15.87 to 41.719) | 29.851 (23.563 to 37.816) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-pertussis toxoid (Anti-PT), anti- filamentous haemagglutinin (Anti-FHA) and anti-pertactin (Anti-PRN) antibody concentrations

| | |
|-----------------|--|
| End point title | Anti-pertussis toxoid (Anti-PT), anti- filamentous haemagglutinin (Anti-FHA) and anti-pertactin (Anti-PRN) antibody concentrations |
|-----------------|--|

End point description:

Anti-PT, Anti-FHA and Anti-PRN concentrations measured by Enzyme-Linked Immunosorbent Assay (ELISA) were calculated, expressed as geometric mean concentrations (GMCs) in ELISA unit per milliliter (EL.U/mL) and tabulated. The seropositivity cut-off for the assay was $\geq 5 \text{ EL.U/mL}$. Antibody concentrations below the cut-off of the assay were given an arbitrary value of half the cut-off for the purpose of GMC calculation. For this endpoint, the analysis was performed on the according-to-protocol cohort for immunogenicity, e. a., evaluable subjects for whom assay results were available for antibodies against at least one study vaccine antigen component after booster vaccination.

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

End point timeframe:

Prior to (PRE) and one month (Month 1) post booster vaccination

| End point values | 10Pn-10Pn Group | 7Pn-7Pn Group | 7Pn-10Pn Group | |
|--|------------------------|------------------------|------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 344 | 46 | 136 | |
| Units: EL.U/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-PT, PRE (N=332;34;133) | 5.5 (5.1 to 6.1) | 7.3 (5.2 to 10.3) | 7 (6.1 to 8.1) | |
| Anti-PT, Month 1 (N=338;46;135) | 79.6 (73.8 to 85.9) | 76 (60.4 to 95.7) | 85.8 (76.9 to 95.7) | |
| Anti-FHA, PRE (N=343;36;135) | 27.1 (24.4 to 30.1) | 29 (20.5 to 40.8) | 35.5 (29.7 to 42.3) | |
| Anti-FHA, Month 1 (N=343;46;136) | 357.7 (332.6 to 384.7) | 334.5 (278.1 to 402.2) | 400.2 (356.4 to 449.5) | |
| Anti-PRN, PRE (N=344;34;136) | 9.1 (8.2 to 10.1) | 11.1 (7.6 to 16.2) | 12.1 (10.1 to 14.6) | |
| Anti-PRN, Month 1 (N=342;45;135) | 248.9 (226.5 to 273.4) | 204.6 (155.8 to 268.7) | 276.5 (239.1 to 319.7) | |

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:

Anti-D and Anti-TT antibody concentrations were calculated, expressed as geometric mean concentrations (GMCs), in International units per milliliter (IU/mL), and tabulated. The seropositivity cut-off for the assay was ≥ 0.1 IU/mL. Antibody concentrations below the cut-off of the assay were given an arbitrary value of half the cut-off for the purpose of GMC calculation. For this endpoint, the analysis was performed on the according-to-protocol cohort for immunogenicity, e. a., evaluable subjects for whom assay results were available for antibodies against at least one study vaccine antigen component after booster vaccination.

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

End point timeframe:

Prior to (PRE) and one month (Month 1) post booster vaccination

| End point values | 10Pn-10Pn Group | 7Pn-7Pn Group | 7Pn-10Pn Group | |
|--|------------------------|------------------------|-------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 344 | 46 | 136 | |
| Units: EL.U/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-D, PRE (N=344;34;136) | 0.179 (0.161 to 0.199) | 0.291 (0.2 to 0.424) | 0.29 (0.25 to 0.336) | |
| Anti-D, Month 1 (N=343;45;136) | 5.809 (5.352 to 6.305) | 6.272 (4.883 to 8.055) | 9.337 (8.419 to 10.356) | |
| Anti-TT, PRE (N=344;35;136) | 0.417 (0.382 to 0.456) | 0.261 (0.187 to 0.364) | 0.265 (0.225 to 0.313) | |

| | | | | |
|---------------------------------|-------------------------|-----------------------|------------------------|--|
| Anti-TT, Month 1 (N=343;46;136) | 9.983 (9.293 to 10.724) | 4.28 (3.294 to 5.562) | 5.677 (5.038 to 6.397) | |
|---------------------------------|-------------------------|-----------------------|------------------------|--|

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:

Anti-HBs antibody concentrations were calculated, expressed as geometric mean concentrations (GMCs), in milli-International unit per milliliter (IU/mL), and tabulated. The seropositivity cut-off for the assay was ≥ 10 mIU/mL. Antibody concentrations below the cut-off of the assay were given an arbitrary value of half the cut-off for the purpose of GMC calculation. For this endpoint, the analysis was performed on the according-to-protocol cohort for immunogenicity, e. a., evaluable subjects for whom assay results were available for antibodies against at least one study vaccine antigen component after booster vaccination.

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

End point timeframe:

Prior to (PRE) and one month (Month 1) post booster vaccination

| End point values | 10Pn-10Pn Group | 7Pn-7Pn Group | 7Pn-10Pn Group | |
|--|---------------------------|---------------------------|---------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 329 | 48 | 134 | |
| Units: mIU/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-HBs, PRE (N=329;48;134) | 147.2 (124.7 to 173.7) | 148.9 (100.4 to 220.8) | 156.6 (125.5 to 195.5) | |
| Anti-HBs, Month 1 (N=325;47;132) | 3869.1 (3218.1 to 4651.8) | 3132.2 (1906.3 to 5146.5) | 4358.6 (3495.5 to 5434.8) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-polio type 1, 2 and 3 (Anti-Polio 1, 2 and 3) antibody titers

| | |
|-----------------|--|
| End point title | Anti-polio type 1, 2 and 3 (Anti-Polio 1, 2 and 3) antibody titers |
|-----------------|--|

End point description:

Anti-Polio 1, 2 and 3 antibody titers were calculated, expressed as geometric mean titers (GMTs) and tabulated. The seroprotection cut-off for the assay was ≥ 8 . Antibody titers below the cut-off of the assay were given an arbitrary value of half the cut-off for the purpose of GMT calculation. For this endpoint, the analysis was performed on the according-to-protocol cohort for immunogenicity, e. a., evaluable subjects for whom assay results were available for antibodies against at least one study vaccine antigen component after booster vaccination.

| | |
|---|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Prior to (PRE) and one month (Month 1) post booster vaccination | |

| End point values | 10Pn-10Pn Group | 7Pn-7Pn Group | 7Pn-10Pn Group | |
|--|-------------------------|--------------------------|---------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 318 | 48 | 131 | |
| Units: Titers | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-Polio 1, PRE (N=318;48;131) | 25.3 (21.9 to 29.3) | 21.2 (15 to 30) | 27.1 (20.7 to 35.4) | |
| Anti-Polio 1, Month 1 (N=279;42;121) | 904.4 (779.7 to 1049.1) | 819.3 (552.9 to 1214.2) | 1003.7 (817.5 to 1232.3) | |
| Anti-Polio 2, PRE (N=317;46;130) | 20.8 (18.1 to 24) | 12.9 (8.8 to 18.9) | 17.9 (14.1 to 22.8) | |
| Anti-Polio 2 , Month 1 (N=280;43;122) | 793.5 (679.7 to 926.3) | 495.7 (300.2 to 818.5) | 661.2 (496.7 to 880.3) | |
| Anti-Polio 3, PRE (N=262;39;113) | 33.7 (28.5 to 39.8) | 25.8 (16.7 to 39.8) | 28.2 (21.6 to 36.8) | |
| Anti-Polio 3, Month 1 (N=270;41;116) | 1465 (1257.1 to 1707.3) | 1191.7 (743.1 to 1911.3) | 1646.5 (1294.4 to 2094.5) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects booster (BST) responder to pertussis toxoid (PT), filamentous haemagglutinin (FHA) and pertactin antigens

| | |
|-----------------|--|
| End point title | Number of subjects booster (BST) responder to pertussis toxoid (PT), filamentous haemagglutinin (FHA) and pertactin antigens |
|-----------------|--|

End point description:

A BST responder to PT, FHA and PRN antigens was defined as a subject with the appearance of antibodies in subjects who were seronegative prior to the booster vaccination or at least 2-fold increase of pre-booster vaccination antibody concentrations in subjects who were seropositive prior to the booster vaccination. A seropositive/seronegative subject as regards Anti-PT/-FHA/ -PRN antibodies was defined as a subject with anti-PT/-FHA/ -PRN antibody concentrations ≥ 5 Enzyme-linked Immunosorbent assay (ELISA) unit per milli-liter (EL.U/mL)

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| One month (Month 1) post booster vaccination | |

| End point values | 10Pn-10Pn Group | 7Pn-7Pn Group | 7Pn-10Pn Group | |
|---|-----------------|-----------------|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 340 | 33 | 135 | |
| Units: Subjects | | | | |
| BST responder to PT antigens (N=324;31;132) | 323 | 31 | 132 | |
| BST responder to FHA antigens (N=340;33;135) | 332 | 31 | 129 | |
| BST responder to PRN antigens (N=340;31;135) | 339 | 30 | 131 | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited local and general symptoms: During the 4 days post booster; Unsolicited AEs: During the 31 days post booster; SAEs: From Month 0 prior to booster vaccination up to Month 6, end of the extended safety follow-up in this study 10PN-PD-DIT-007

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 | 10.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-----------------|
| Reporting group title | 10Pn-10Pn Group |
|-----------------------|-----------------|

Reporting group description:

This group consisted of subjects previously vaccinated with the 10Pn-PD-DiT vaccine (also referred as 10Pn vaccine or Synflorix™) as part of a previous study by GSK Biologicals – the 10PN-PD-DIT-001 (105553) study (EuDRA-CT number: 2005-003300-11). As part of the 105553 study, subjects had received a 3-dose primary vaccination of 10Pn vaccine at 2, 3 and 4 months of age (injected intramuscularly [IM] in the right thigh) co-administered with DTPa-HBV-IPV/Hib vaccine (or Infanrix hexa™), except for the second dose in France, which was co-administered with DTPa-IPV/Hib (or Infanrix™ IPV Hib), injected intramuscularly in the left thigh. As part of this study, at 12-18 months of age, subjects received a booster dose of 10Pn vaccine, injected IM in the right thigh or deltoid, co-administered with DTPa-HBV-IPV/Hib vaccine, injected IM in the left thigh or deltoid.

| | |
|-----------------------|----------------|
| Reporting group title | 7Pn-10Pn Group |
|-----------------------|----------------|

Reporting group description:

This group consisted of subjects previously vaccinated with the 7Pn vaccine (also referred as Prevenar™) as part of a previous study by GSK Biologicals – the 10PN-PD-DIT-001 (105553) study (EuDRA-CT number: 2005-003300-11). As part of the 105553 study, subjects had received a 3-dose primary vaccination of 7Pn vaccine at 2, 3 and 4 months of age (injected intramuscularly [IM] in the right thigh) co-administered with DTPa-HBV-IPV/Hib vaccine (or Infanrix hexa™), except for the second dose in France, which was co-administered with DTPa-IPV/Hib (or Infanrix™ IPV Hib), injected intramuscularly in the left thigh. As part of this study, at 12-18 months of age, subjects received a booster dose of 10Pn-PD-DiT vaccine (also referred as 10Pn vaccine or Synflorix™), injected IM in the right thigh or deltoid, co-administered with DTPa-HBV-IPV/Hib vaccine, injected IM in the left thigh or deltoid.

| | |
|-----------------------|---------------|
| Reporting group title | 7Pn-7Pn Group |
|-----------------------|---------------|

Reporting group description:

This group consisted of subjects previously vaccinated with the 7Pn vaccine (also referred as Prevenar™) as part of a previous study by GSK Biologicals – the 10PN-PD-DIT-001 (105553) study (EuDRA-CT number: 2005-003300-11). As part of the 105553 study, subjects had received a 3-dose primary vaccination of 7Pn vaccine at 2, 3 and 4 months of age (injected intramuscularly [IM] in the right thigh) co-administered with DTPa-HBV-IPV/Hib vaccine (or Infanrix hexa™), except for the second dose in France, which was co-administered with DTPa-IPV/Hib (or Infanrix™ IPV Hib), injected intramuscularly in the left thigh. As part of this study, at 12-18 months of age, subjects received a booster dose of 7Pn vaccine, injected IM in the right thigh or deltoid, co-administered with DTPa-HBV-IPV/Hib vaccine, injected IM in the left thigh or deltoid.

| Serious adverse events | 10Pn-10Pn Group | 7Pn-10Pn Group | 7Pn-7Pn Group |
|---|------------------|-----------------|----------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 33 / 737 (4.48%) | 8 / 283 (2.83%) | 6 / 92 (6.52%) |
| number of deaths (all causes) | 0 | 0 | 0 |

| | | | |
|---|---|-----------------|----------------|
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| Drug toxicity (post booster) | Additional description: SAE reported within the 31 days after the booster | | |
| subjects affected / exposed | 1 / 737 (0.14%) | 0 / 283 (0.00%) | 0 / 92 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Concussion (til study end) | Additional description: SAE reported within the 31 days after the booster and during the ESFU, based on subjects participating for the ESFU phase | | |
| alternative dictionary used: MedDRA 11.0 | | | |
| subjects affected / exposed ^[1] | 1 / 726 (0.14%) | 0 / 282 (0.00%) | 0 / 91 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Drug toxicity (til study end) | Additional description: SAE reported within the 31 days after the booster and during the ESFU, based on subjects participating for the ESFU phase | | |
| alternative dictionary used: MedDRA 11.0 | | | |
| subjects affected / exposed ^[2] | 1 / 726 (0.14%) | 0 / 282 (0.00%) | 0 / 91 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Limb injury (til study end) | Additional description: SAE reported within the 31 days after the booster and during the ESFU, based on subjects participating for the ESFU phase | | |
| alternative dictionary used: MedDRA 11.0 | | | |
| subjects affected / exposed ^[3] | 1 / 726 (0.14%) | 0 / 282 (0.00%) | 0 / 91 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thermal burn (til study end) | Additional description: SAE reported within the 31 days after the booster and during the ESFU, based on subjects participating for the ESFU phase | | |
| alternative dictionary used: MedDRA 11.0 | | | |
| subjects affected / exposed ^[4] | 0 / 726 (0.00%) | 0 / 282 (0.00%) | 1 / 91 (1.10%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Febrile convulsion (post booster) | Additional description: SAE reported within the 31 days after the booster | | |
| subjects affected / exposed | 1 / 737 (0.14%) | 0 / 283 (0.00%) | 0 / 92 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Febrile convulsion (til study end) | Additional description: SAE reported within the 31 days after the booster and during the ESFU, based on subjects participating for the ESFU phase | | |

| | | | |
|---|---|-----------------|----------------|
| alternative dictionary used: MedDRA 11.0 | | | |
| subjects affected / exposed ^[5] | 2 / 726 (0.28%) | 0 / 282 (0.00%) | 0 / 91 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Microcytic anaemia (post booster) | Additional description: SAE reported within the 31 days after the booster | | |
| subjects affected / exposed | 1 / 737 (0.14%) | 0 / 283 (0.00%) | 0 / 92 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Microcytic anaemia(til study end) | Additional description: SAE reported within the 31 days after the booster and during the ESFU, based on subjects participating for the ESFU phase | | |
| alternative dictionary used: MedDRA 11.0 | | | |
| subjects affected / exposed ^[6] | 1 / 726 (0.14%) | 0 / 282 (0.00%) | 0 / 91 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Oedema peripheral (post booster) | Additional description: SAE reported within the 31 days after the booster | | |
| subjects affected / exposed | 0 / 737 (0.00%) | 1 / 283 (0.35%) | 0 / 92 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oedema peripheral (til study end) | Additional description: SAE reported within the 31 days after the booster and during the ESFU, based on subjects participating for the ESFU phase | | |
| alternative dictionary used: MedDRA 11.0 | | | |
| subjects affected / exposed ^[7] | 0 / 726 (0.00%) | 1 / 282 (0.35%) | 0 / 91 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Gastritis (post booster) | Additional description: SAE reported within the 31 days after the booster | | |
| subjects affected / exposed | 1 / 737 (0.14%) | 0 / 283 (0.00%) | 0 / 92 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diarrhoea (til study end) | Additional description: SAE reported within the 31 days after the booster and during the ESFU, based on subjects participating for the ESFU phase | | |
| alternative dictionary used: MedDRA 11.0 | | | |

| | | | |
|---|---|-----------------|----------------|
| subjects affected / exposed ^[8] | 1 / 726 (0.14%) | 0 / 282 (0.00%) | 1 / 91 (1.10%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastritis (til study end) | Additional description: SAE reported within the 31 days after the booster and during the ESFU, based on subjects participating for the ESFU phase | | |
| alternative dictionary used: MedDRA 11.0 | | | |
| subjects affected / exposed ^[9] | 1 / 726 (0.14%) | 0 / 282 (0.00%) | 0 / 91 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Stomatitis (til study end) | Additional description: SAE reported within the 31 days after the booster and during the ESFU, based on subjects participating for the ESFU phase | | |
| alternative dictionary used: MedDRA 11.0 | | | |
| subjects affected / exposed ^[10] | 1 / 726 (0.14%) | 0 / 282 (0.00%) | 0 / 91 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Asthma (post booster) | Additional description: SAE reported within the 31 days after the booster | | |
| subjects affected / exposed | 1 / 737 (0.14%) | 0 / 283 (0.00%) | 0 / 92 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchitis chronic (post booster) | Additional description: SAE reported within the 31 days after the booster | | |
| subjects affected / exposed | 0 / 737 (0.00%) | 2 / 283 (0.71%) | 0 / 92 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Asthma (til study end) | Additional description: SAE reported within the 31 days after the booster and during the ESFU, based on subjects participating for the ESFU phase | | |
| alternative dictionary used: MedDRA 11.0 | | | |
| subjects affected / exposed ^[11] | 1 / 726 (0.14%) | 0 / 282 (0.00%) | 0 / 91 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchitis chronic (til study end) | Additional description: SAE reported within the 31 days after the booster and during the ESFU, based on subjects participating for the ESFU phase | | |
| alternative dictionary used: MedDRA 11.0 | | | |
| subjects affected / exposed ^[12] | 6 / 726 (0.83%) | 4 / 282 (1.42%) | 0 / 91 (0.00%) |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 4 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|-----------------|----------------|
| Skin and subcutaneous tissue disorders | | | |
| Dermatitis atopic (post booster) | | | |
| Additional description: SAE reported within the 31 days after the booster | | | |
| subjects affected / exposed | 1 / 737 (0.14%) | 0 / 283 (0.00%) | 0 / 92 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dermatitis atopic (til study end) | | | |
| Additional description: SAE reported within the 31 days after the booster and during the ESFU, based on subjects participating for the ESFU phase | | | |
| alternative dictionary used: MedDRA 11.0 | | | |
| subjects affected / exposed ^[13] | 1 / 726 (0.14%) | 0 / 282 (0.00%) | 0 / 91 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Purpura (til study end) | | | |
| Additional description: SAE reported within the 31 days after the booster and during the ESFU, based on subjects participating for the ESFU phase | | | |
| alternative dictionary used: MedDRA 11.0 | | | |
| subjects affected / exposed ^[14] | 1 / 726 (0.14%) | 0 / 282 (0.00%) | 0 / 91 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Bronchitis (post booster) | | | |
| Additional description: SAE reported within the 31 days after the booster | | | |
| subjects affected / exposed | 1 / 737 (0.14%) | 1 / 283 (0.35%) | 1 / 92 (1.09%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ear infection (post booster) | | | |
| Additional description: SAE reported within the 31 days after the booster | | | |
| subjects affected / exposed | 0 / 737 (0.00%) | 0 / 283 (0.00%) | 1 / 92 (1.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis (post booster) | | | |
| Additional description: SAE reported within the 31 days after the booster | | | |
| subjects affected / exposed | 3 / 737 (0.41%) | 1 / 283 (0.35%) | 0 / 92 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis rotavirus (post booster) | | | |
| Additional description: SAE reported within the 31 days after the booster | | | |
| subjects affected / exposed | 1 / 737 (0.14%) | 0 / 283 (0.00%) | 0 / 92 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Laryngitis (post booster) | | | |
| Additional description: SAE reported within the 31 days after the booster | | | |

| | | | |
|--|---|-----------------|----------------|
| subjects affected / exposed | 0 / 737 (0.00%) | 0 / 283 (0.00%) | 1 / 92 (1.09%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nasopharyngitis (post booster) | Additional description: SAE reported within the 31 days after the booster | | |
| subjects affected / exposed | 0 / 737 (0.00%) | 1 / 283 (0.35%) | 0 / 92 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pharyngitis (post booster) | Additional description: SAE reported within the 31 days after the booster | | |
| subjects affected / exposed | 2 / 737 (0.27%) | 0 / 283 (0.00%) | 0 / 92 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia (post booster) | Additional description: SAE reported within the 31 days after the booster | | |
| subjects affected / exposed | 1 / 737 (0.14%) | 0 / 283 (0.00%) | 0 / 92 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory tract infection (post booster) | Additional description: SAE reported within the 31 days after the booster | | |
| subjects affected / exposed | 1 / 737 (0.14%) | 0 / 283 (0.00%) | 0 / 92 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Upper respiratory tract infection (post booster) | Additional description: SAE reported within the 31 days after the booster | | |
| subjects affected / exposed | 1 / 737 (0.14%) | 0 / 283 (0.00%) | 0 / 92 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Adenovirus infection (til study end) | Additional description: SAE reported within the 31 days after the booster and during the ESFU, based on subjects participating for the ESFU phase | | |
| alternative dictionary used: MedDRA 11.0 | | | |
| subjects affected / exposed ^[15] | 1 / 726 (0.14%) | 0 / 282 (0.00%) | 0 / 91 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchiolitis (til study end) | Additional description: SAE reported within the 31 days after the booster and during the ESFU, based on subjects participating for the ESFU phase | | |
| alternative dictionary used: MedDRA 11.0 | | | |

| | | | |
|---|---|-----------------|----------------|
| subjects affected / exposed ^[16] | 0 / 726 (0.00%) | 0 / 282 (0.00%) | 1 / 91 (1.10%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchitis (til study end) | Additional description: SAE reported within the 31 days after the booster and during the ESFU, based on subjects participating for the ESFU phase | | |
| alternative dictionary used: MedDRA 11.0 | | | |
| subjects affected / exposed ^[17] | 2 / 726 (0.28%) | 2 / 282 (0.71%) | 1 / 91 (1.10%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ear infection (til study end) | Additional description: SAE reported within the 31 days after the booster and during the ESFU, based on subjects participating for the ESFU phase | | |
| alternative dictionary used: MedDRA 11.0 | | | |
| subjects affected / exposed ^[18] | 0 / 726 (0.00%) | 0 / 282 (0.00%) | 1 / 91 (1.10%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis rotavirus (til study end) | Additional description: SAE reported within the 31 days after the booster and during the ESFU, based on subjects participating for the ESFU phase | | |
| alternative dictionary used: MedDRA 11.0 | | | |
| subjects affected / exposed ^[19] | 1 / 726 (0.14%) | 1 / 282 (0.35%) | 1 / 91 (1.10%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Laryngitis (til study end) | Additional description: SAE reported within the 31 days after the booster and during the ESFU, based on subjects participating for the ESFU phase | | |
| alternative dictionary used: MedDRA 11.0 | | | |
| subjects affected / exposed ^[20] | 1 / 726 (0.14%) | 0 / 282 (0.00%) | 2 / 91 (2.20%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nasopharyngitis (til study end) | Additional description: SAE reported within the 31 days after the booster and during the ESFU, based on subjects participating for the ESFU phase | | |
| alternative dictionary used: MedDRA 11.0 | | | |
| subjects affected / exposed ^[21] | 1 / 726 (0.14%) | 1 / 282 (0.35%) | 0 / 91 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Otitis media (til study end) | Additional description: SAE reported within the 31 days after the booster and during the ESFU, based on subjects participating for the ESFU phase | | |
| alternative dictionary used: MedDRA 11.0 | | | |

| | | | |
|---|---|-----------------|----------------|
| subjects affected / exposed ^[22] | 0 / 726 (0.00%) | 1 / 282 (0.35%) | 0 / 91 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pharyngitis (til study end) | Additional description: SAE reported within the 31 days after the booster and during the ESFU, based on subjects participating for the ESFU phase | | |
| alternative dictionary used: MedDRA 11.0 | | | |
| subjects affected / exposed ^[23] | 2 / 726 (0.28%) | 0 / 282 (0.00%) | 0 / 91 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia (til study end) | Additional description: SAE reported within the 31 days after the booster and during the ESFU, based on subjects participating for the ESFU phase | | |
| alternative dictionary used: MedDRA 11.0 | | | |
| subjects affected / exposed ^[24] | 2 / 726 (0.28%) | 0 / 282 (0.00%) | 0 / 91 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyelonephritis (til study end) | Additional description: SAE reported within the 31 days after the booster and during the ESFU, based on subjects participating for the ESFU phase | | |
| alternative dictionary used: MedDRA 11.0 | | | |
| subjects affected / exposed ^[25] | 1 / 726 (0.14%) | 0 / 282 (0.00%) | 0 / 91 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory tract infection (til study end) | Additional description: SAE reported within the 31 days after the booster and during the ESFU, based on subjects participating for the ESFU phase | | |
| alternative dictionary used: MedDRA 11.0 | | | |
| subjects affected / exposed ^[26] | 1 / 726 (0.14%) | 1 / 282 (0.35%) | 0 / 91 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Upper respiratory tract infection (til study end) | Additional description: : SAE reported within the 31 days after the booster and during the ESFU, based on subjects participating for the ESFU phase | | |
| alternative dictionary used: MedDRA 11.0 | | | |
| subjects affected / exposed ^[27] | 1 / 726 (0.14%) | 0 / 282 (0.00%) | 0 / 91 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis (til study end) | | | |
| alternative dictionary used: MedDRA 11.0 | | | |

| | | | |
|---|---|-----------------|----------------|
| subjects affected / exposed ^[28] | 9 / 726 (1.24%) | 1 / 282 (0.35%) | 0 / 91 (0.00%) |
| occurrences causally related to treatment / all | 0 / 9 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Dehydration (post booster) | Additional description: SAE reported within the 31 days after the booster | | |
| subjects affected / exposed | 1 / 737 (0.14%) | 0 / 283 (0.00%) | 0 / 92 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dehydration (til study end) | Additional description: SAE reported within the 31 days after the booster and during the ESFU, based on subjects participating for the ESFU phase | | |
| alternative dictionary used: MedDRA 11.0 | | | |
| subjects affected / exposed ^[29] | 1 / 726 (0.14%) | 0 / 282 (0.00%) | 0 / 91 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Weight gain poor (til study end) | Additional description: SAE reported within the 31 days after the booster and during the ESFU, based on subjects participating for the ESFU phase | | |
| alternative dictionary used: MedDRA 11.0 | | | |
| subjects affected / exposed ^[30] | 1 / 726 (0.14%) | 0 / 282 (0.00%) | 0 / 91 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

Notes:

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

Justification: Analysis for this event was performed on subjects analysed and/or available results.

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

Justification: Analysis for this event was performed on subjects analysed and/or available results.

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

Justification: Analysis for this event was performed on subjects analysed and/or available results.

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

Justification: Analysis for this event was performed on subjects analysed and/or available results.

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

Justification: Analysis for this event was performed on subjects analysed and/or available results.

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

Justification: Analysis for this event was performed on subjects analysed and/or available results.

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

Justification: Analysis for this event was performed on subjects analysed and/or available results.

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

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

Justification: Analysis for this event was performed on subjects analysed and/or available results.

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Justification: Analysis for this event was performed on subjects analysed and/or available results.

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

| Non-serious adverse events | 10Pn-10Pn Group | 7Pn-10Pn Group | 7Pn-7Pn Group |
|---|--------------------|--------------------|------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 452 / 737 (61.33%) | 176 / 283 (62.19%) | 59 / 92 (64.13%) |
| General disorders and administration site conditions | | | |
| Pain | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed ^[31] | 452 / 735 (61.50%) | 150 / 282 (53.19%) | 48 / 91 (52.75%) |
| occurrences (all) | 452 | 150 | 48 |
| Redness | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed ^[32] | 451 / 735 (61.36%) | 153 / 282 (54.26%) | 59 / 91 (64.84%) |
| occurrences (all) | 451 | 153 | 59 |
| Swelling | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed ^[33] | 338 / 735 (45.99%) | 112 / 282 (39.72%) | 42 / 91 (46.15%) |
| occurrences (all) | 338 | 112 | 42 |
| Drowsiness | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed ^[34] | 303 / 735 (41.22%) | 130 / 282 (46.10%) | 48 / 91 (52.75%) |
| occurrences (all) | 303 | 130 | 48 |
| Fever (rectal temperature $\geq 38^{\circ}\text{C}$) | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed ^[35] | 245 / 735 (33.33%) | 112 / 282 (39.72%) | 33 / 91 (36.26%) |
| occurrences (all) | 245 | 112 | 33 |
| Irritability | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed ^[36] | 438 / 735 (59.59%) | 176 / 282 (62.41%) | 55 / 91 (60.44%) |
| occurrences (all) | 438 | 176 | 55 |
| Loss of appetite | | | |
| alternative assessment type: Systematic | | | |

| | | | |
|---|--------------------|-------------------|------------------|
| subjects affected / exposed ^[37] | 230 / 735 (31.29%) | 92 / 282 (32.62%) | 31 / 91 (34.07%) |
| occurrences (all) | 230 | 92 | 31 |
| Injection site induration | | | |
| subjects affected / exposed | 1 / 737 (0.14%) | 7 / 283 (2.47%) | 7 / 92 (7.61%) |
| occurrences (all) | 1 | 7 | 7 |
| Infections and infestations | | | |
| Rhinitis | | | |
| subjects affected / exposed | 28 / 737 (3.80%) | 19 / 283 (6.71%) | 4 / 92 (4.35%) |
| occurrences (all) | 28 | 19 | 4 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 25 / 737 (3.39%) | 13 / 283 (4.59%) | 5 / 92 (5.43%) |
| occurrences (all) | 25 | 13 | 5 |

Notes:

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

Justification: Analysis for this event was performed on subjects analysed and/or available results.

[32] - 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.

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[33] - 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.

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

Justification: Analysis for this event was performed on subjects analysed and/or available results.

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

Justification: Analysis for this event was performed on subjects analysed and/or available results.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported