# Clinical trial results:
# Assessment of long-term antibody persistence and immunological memory in children previously vaccinated with four pneumococcal conjugate vaccine doses and assessment of pneumococcal catch-up vaccination with GSK1024850A at 5 years of age.

## Summary

| | |
|---|---|
| EudraCT number | 2007-005392-34 |
| Trial protocol | PL |
| Global end of trial date | 21 November 2011 |

### Results information

| | |
|---|---|
| Result version number | v4 |
| This version publication date | 04 November 2020 |
| First version publication date | 30 July 2015 |
| Version creation reason | • Correction of full data set<br>Results have been amended to account for consistency with other registries. |

## Trial information

### Trial identification

| | |
|---|---|
| Sponsor protocol code | 111345 |

### Additional study identifiers

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

Notes:

### Sponsors

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

Notes:

### Paediatric regulatory details

| | |
|---|---|
| Is trial part of an agreed paediatric investigation plan (PIP) | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | Yes |

Notes:

## Results analysis stage

| | |
|---|---|
| Analysis stage | Final |
| Date of interim/final analysis | 14 October 2013 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 21 November 2011 |
| Global end of trial reached? | Yes |
| Global end of trial date | 21 November 2011 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

To assess antibody persistence in children previously vaccinated with four doses of pneumococcal conjugate vaccine in primary vaccination study 10PN-PD-DIT-001 and booster vaccination study 10PN-PD-DIT-007.

Protection of trial subjects:

The vaccinees was observed closely for at least 30 minutes following the administration of vaccine, with appropriate medical treatment readily available in case of a rare anaphylactic reaction.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 03 March 2008 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Poland: 524 |
| Worldwide total number of subjects | 524 |
| EEA total number of subjects | 524 |

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) | 0 |
| Children (2-11 years) | 524 |
| 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:

Primed groups included Synflorix vaccinated subjects in study 10PN-PD-DIT-007. The Unprimed Group, added only in Year 4,included subjects unprimed with any pneumococcal vaccine age-matched with primed groups. The study included 3 sub-studies (111345, 111346, 111347) corresponding to Year 1, 2 and 4 time points post Dose 1 in Study 10PN-PD-DIT-001.

### Pre-assignment

Screening details:

At screening, subjects with previous participation in 10PN-PD-DIT-007 study were invited to join this study. Informed consent was obtained and signed from subjects' parents/guardians, check for inclusion/exclusion criteria and contraindications/precautions was performed, and medical history of subjects was collected.

### Period 1

| | |
|---|---|
| Period 1 title | Follow-up Period: Year 1 |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Synflorix + Infanrix + Havrix and/or Varilrix Group |

Arm description:

This group consisted of subjects primed with Synflorix vaccine in the 10PN-PD-DIT-001 (1105553) and 007 (107046) studies. In 105553 study, subjects had been primed with 3 doses of Synflorix vaccine at 2, 3 and 4 months of age co-administered with Infanrix related vaccines. In 107046 study, subjects had received a booster dose of Synflorix vaccine at 12-18 months of age co-administered with Infanrix hexa vaccine. In this study, in the Year 4 (111347 study), subjects received at Month 48 (4 years post Dose 1 in study 105553) one additional dose of Synflorix vaccine. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix) and/or against varicella (a single dose of Varilrix).

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

Dosage and administration details:

3 doses in primary vaccination study 10PN-PD-DT-001 (1105553); 1 dose in booster vaccination study 10PN-PD-DIT-007 (107046);

| | |
|---|---|
| Investigational medicinal product name | Havrix |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Two doses were proposed post blood sampling procedure to subjects from all three primed groups.

| | |
|---|---|
| Investigational medicinal product name | Varilrix |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder and solvent for solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

One dose was proposed post blood sampling procedure to subjects from all three primed groups.

| **Arm title** | Prevenar + Infanrix + Havrix and/or Varilrix Group |
|---|---|

Arm description:

This group consisted of subjects vaccinated with Prevenar vaccine in the 10PN-PD-DIT-001 (105553) and 007 (107046) studies. In 105553 study, subjects had been primed with 3 doses of Prevenar vaccine at 2, 3 and 4 months of age co-administered with Infanrix related vaccines. In 107046 study, subjects had received a booster dose at 12-18 months of age of Prevenar vaccine co-administered with Infanrix hexa vaccine. In this study, in the Year 4 111347 study, subjects had received at Month 48 (4 years post Dose 1 in study 105553) one dose of Synflorix vaccine. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix and/or against varicella (a single dose of Varilrix).

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Prevenar |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

3 doses in primary vaccination study 10PN-PD-DT-001 (1105553); 1 dose in booster vaccination study 10PN-PD-DIT-007 (107046)

| | |
|---|---|
| Investigational medicinal product name | Havrix |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Two doses were proposed post blood sampling procedure to subjects from all three primed groups.

| | |
|---|---|
| Investigational medicinal product name | Varilrix |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder and solvent for solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

One dose was proposed post blood sampling procedure to subjects from all three primed groups.

| **Arm title** | Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix |
|---|---|

Arm description:

This group consisted of subjects vaccinated with Prevenar and Synflorix vaccines in the 10PN-PD-DIT-001 (105553) and 10PN-PD-DIT-007 (107046) studies. In 105553 study, subjects had been primed with 3 doses Prevenar vaccine at 2, 3 and 4 months of age co-administered with Infanrix related vaccines. In the 107046 study, subjects had received at 12-18 months of age a booster dose of Synflorix vaccine co-administered with Infanrix hexa vaccine. In this study, in the Year 4 (111347 study), subjects had received at Month 48 (4 years post Dose 1 in study 105553) one additional dose of Synflorix vaccine. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix and/or against varicella (a single dose of Varilrix).

| | |
|---|---|
| Arm type | Control |
| Investigational medicinal product name | Prevenar |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

3 doses in primary vaccination study 10PN-PD-DT-001 (1105553)

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

Dosage and administration details:

1 dose in booster study 10PN-PD-DIT-007 (107046)

| | |
|---|---|
| Investigational medicinal product name | Havrix |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Two doses were proposed post blood sampling procedure to subjects from all three primed groups.

| | |
|---|---|
| Investigational medicinal product name | Varilrix |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder and solvent for solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

One dose was proposed post blood sampling procedure to subjects from all three primed groups.

| **Number of subjects in period 1** | Synflorix + Infanrix + Havrix and/or Varilrix Group | Prevenar + Infanrix + Havrix and/or Varilrix Group | Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix |
|---|---|---|---|
| Started | 391 | 31 | 102 |
| Completed | 391 | 31 | 102 |

## Period 2

| | |
|---|---|
| Period 2 title | Follow-up Period: Year 2 |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

## Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Synflorix + Infanrix + Havrix and/or Varilrix Group |

Arm description:

This group consisted of subjects primed with Synflorix vaccine in the 10PN-PD-DIT-001 (1105553) and 007 (107046) studies. In 105553 study, subjects had been primed with 3 doses of Synflorix vaccine at 2, 3 and 4 months of age co-administered with Infanrix related vaccines. In 107046 study, subjects had received a booster dose of Synflorix vaccine at 12-18 months of age co-administered with Infanrix hexa vaccine. In this study, in the Year 4 (111347 study), subjects received at Month 48 (4 years post Dose 1 in study 105553) one additional dose of Synflorix vaccine. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix) and/or against varicella (a single dose of Varilrix).

| | |
|---|---|
| Arm type | Experimental |

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

Dosage and administration details:

3 doses in primary vaccination study 10PN-PD-DT-001 (1105553); 1 dose in booster vaccination study 10PN-PD-DIT-007 (107046);

| | |
|---|---|
| Investigational medicinal product name | Havrix |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Two doses were proposed post blood sampling procedure to subjects from all three primed groups.

| | |
|---|---|
| Investigational medicinal product name | Varilrix |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder and solvent for solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

One dose was proposed post blood sampling procedure to subjects from all three primed groups.

| | |
|---|---|
| **Arm title** | Prevenar + Infanrix + Havrix and/or Varilrix Group |

Arm description:

This group consisted of subjects vaccinated with Prevenar vaccine in the 10PN-PD-DIT-001 (105553) and 007 (107046) studies. In 105553 study, subjects had been primed with 3 doses of Prevenar vaccine at 2, 3 and 4 months of age co-administered with Infanrix related vaccines. In 107046 study, subjects had received a booster dose at 12-18 months of age of Prevenar vaccine co-administered with Infanrix hexa vaccine. In this study, in the Year 4 111347 study, subjects had received at Month 48 (4 years post Dose 1 in study 105553) one dose of Synflorix vaccine. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix and/or against varicella (a single dose of Varilrix).

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Prevenar |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

3 doses in primary vaccination study 10PN-PD-DT-001 (1105553); 1 dose in booster vaccination study 10PN-PD-DIT-007 (107046)

| | |
|---|---|
| Investigational medicinal product name | Havrix |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Two doses were proposed post blood sampling procedure to subjects from all three primed groups.

| | |
|---|---|
| Investigational medicinal product name | Varilrix |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder and solvent for solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

One dose was proposed post blood sampling procedure to subjects from all three primed groups.

| **Arm title** | Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix |
|---|---|

Arm description:

This group consisted of subjects vaccinated with Prevenar and Synflorix vaccines in the 10PN-PD-DIT-001 (105553) and 10PN-PD-DIT-007 (107046) studies. In 105553 study, subjects had been primed with 3 doses Prevenar vaccine at 2, 3 and 4 months of age co-administered with Infanrix related vaccines. In the 107046 study, subjects had received at 12-18 months of age a booster dose of Synflorix vaccine co-administered with Infanrix hexa vaccine. In this study, in the Year 4 (111347 study), subjects had received at Month 48 (4 years post Dose 1 in study 105553) one additional dose of Synflorix vaccine. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix and/or against varicella (a single dose of Varilrix).

| Arm type | Control |
|---|---|
| Investigational medicinal product name | Prevenar |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

3 doses in primary vaccination study 10PN-PD-DT-001 (1105553)

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

Dosage and administration details:

1 dose in booster study 10PN-PD-DIT-007 (107046)

| Investigational medicinal product name | Havrix |
|---|---|
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Two doses were proposed post blood sampling procedure to subjects from all three primed groups.

| Investigational medicinal product name | Varilrix |
|---|---|
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder and solvent for solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

One dose was proposed post blood sampling procedure to subjects from all three primed groups.

| **Number of subjects in period 2[1]** | Synflorix + Infanrix + Havrix and/or Varilrix Group | Prevenar + Infanrix + Havrix and/or Varilrix Group | Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix |
|---|---|---|---|
| Started | 370 | 31 | 96 |
| Completed | 370 | 31 | 96 |

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Out of the 524 subjects who participated to the year 1 persistence analysis in study 111345, 497 returned participating to the year 2 persistence analysis in study 111346 and 27 were lost to follow up.

## Period 3

| | |
|---|---|
| Period 3 title | Follow-up Period: Year 4 Persistence |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

## Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Synflorix + Infanrix + Havrix and/or Varilrix Group |

Arm description:

This group consisted of subjects primed with Synflorix vaccine in the 10PN-PD-DIT-001 (1105553) and 007 (107046) studies. In 105553 study, subjects had been primed with 3 doses of Synflorix vaccine at 2, 3 and 4 months of age co-administered with Infanrix related vaccines. In 107046 study, subjects had received a booster dose of Synflorix vaccine at 12-18 months of age co-administered with Infanrix hexa vaccine. In this study, in the Year 4 (111347 study), subjects received at Month 48 (4 years post Dose 1 in study 105553) one additional dose of Synflorix vaccine. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix) and/or against varicella (a single dose of Varilrix).

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | 10Pn-PD-DiT |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Route of administration not applicable |

Dosage and administration details:

4 doses received in primary vaccination study 10PN-PD-DT-001 (1105553) and in booster vaccination study 10PN-PD-DIT-007 (107046); 1 dose during this study at follow-up visit (Visit 3)

| | |
|---|---|
| **Arm title** | Prevenar + Infanrix + Havrix and/or Varilrix Group |

Arm description:

This group consisted of subjects vaccinated with Prevenar vaccine in the 10PN-PD-DIT-001 (105553) and 007 (107046) studies. In 105553 study, subjects had been primed with 3 doses of Prevenar vaccine at 2, 3 and 4 months of age co-administered with Infanrix related vaccines. In 107046 study, subjects had received a booster dose at 12-18 months of age of Prevenar vaccine co-administered with Infanrix hexa vaccine. In this study, in the Year 4 111347 study, subjects had received at Month 48 (4 years post Dose 1 in study 105553) one dose of Synflorix vaccine. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix and/or against varicella (a single dose of Varilrix).

| | |
|---|---|
| Arm type | Control |
| Investigational medicinal product name | Prevenar |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

4 doses received in primary vaccination study 10PN-PD-DT-001 (1105553) and in booster vaccination study 10PN-PD-DIT-007 (107046)

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

Dosage and administration details:

1 dose at follow-up visit (Visit 3)

| Arm title | Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix |
|---|---|

Arm description:

This group consisted of subjects vaccinated with Prevenar and Synflorix vaccines in the 10PN-PD-DIT-001 (105553) and 10PN-PD-DIT-007 (107046) studies. In 105553 study, subjects had been primed with 3 doses Prevenar vaccine at 2, 3 and 4 months of age co-administered with Infanrix related vaccines. In the 107046 study, subjects had received at 12-18 months of age a booster dose of Synflorix vaccine co-administered with Infanrix hexa vaccine. In this study, in the Year 4 (111347 study), subjects had received at Month 48 (4 years post Dose 1 in study 105553) one additional dose of Synflorix vaccine. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix and/or against varicella (a single dose of Varilrix).

| Arm type | Experimental |
|---|---|
| Investigational medicinal product name | Prevenar |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

3 doses received in primary vaccination study 10PN-PD-DT-001 (1105553)

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

Dosage and administration details:

1 dose in booster study 10PN-PD-DIT-007 (107046); 1 dose during this study at follow-up visit (Visit 3)

| **Number of subjects in period 3[2]** | Synflorix + Infanrix + Havrix and/or Varilrix Group | Prevenar + Infanrix + Havrix and/or Varilrix Group | Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix |
|---|---|---|---|
| Started | 316 | 25 | 85 |
| Completed | 316 | 25 | 85 |

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Out of the 497 subjects who participated to the year 2 persistence analysis in study 111346, 426 returned participating to the year 4 persistence analysis in study 111347 and 71 were lost to follow up.

## Period 4

| Period 4 title | Follow-up Period: Year 4 Immunogenicity |
|---|---|
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

## Arms

| Are arms mutually exclusive? | Yes |
|---|---|

| **Arm title** | Synflorix + Infanrix + Havrix and/or Varilrix Group |
|---|---|

Arm description:

This group consisted of subjects primed with Synflorix vaccine in the 10PN-PD-DIT-001 (1105553) and 007 (107046) studies. In 105553 study, subjects had been primed with 3 doses of Synflorix vaccine at 2, 3 and 4 months of age co-administered with Infanrix related vaccines. In 107046 study, subjects had received a booster dose of Synflorix vaccine at 12-18 months of age co-administered with Infanrix hexa vaccine. In this study, in the Year 4 (111347 study), subjects received at Month 48 (4 years post Dose 1 in study 105553) one additional dose of Synflorix vaccine. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix) and/or against varicella (a single dose of Varilrix).

| Arm type | Experimental |
|---|---|
| Investigational medicinal product name | 10Pn-PD-DiT |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Route of administration not applicable |

Dosage and administration details:

4 doses received in primary vaccination study 10PN-PD-DT-001 (1105553) and in booster vaccination study 10PN-PD-DIT-007 (107046); 1 dose during this study at follow-up visit (Visit 3)

| **Arm title** | Prevenar + Infanrix + Havrix and/or Varilrix Group |
|---|---|

Arm description:

This group consisted of subjects vaccinated with Prevenar vaccine in the 10PN-PD-DIT-001 (105553) and 007 (107046) studies. In 105553 study, subjects had been primed with 3 doses of Prevenar vaccine at 2, 3 and 4 months of age co-administered with Infanrix related vaccines. In 107046 study, subjects had received a booster dose at 12-18 months of age of Prevenar vaccine co-administered with Infanrix hexa vaccine. In this study, in the Year 4 111347 study, subjects had received at Month 48 (4 years post Dose 1 in study 105553) one dose of Synflorix vaccine. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix and/or against varicella (a single dose of Varilrix).

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

Dosage and administration details:

1 dose at follow-up visit (Visit 3)

| Investigational medicinal product name | Prevenar |
|---|---|
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

4 doses received in primary vaccination study 10PN-PD-DT-001 (1105553) and in booster vaccination study 10PN-PD-DIT-007 (107046)

| **Arm title** | Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix |
|---|---|

Arm description:

This group consisted of subjects vaccinated with Prevenar and Synflorix vaccines in the 10PN-PD-DIT-001 (105553) and 10PN-PD-DIT-007 (107046) studies. In 105553 study, subjects had been primed with 3 doses Prevenar vaccine at 2, 3 and 4 months of age co-administered with Infanrix related vaccines. In the 107046 study, subjects had received at 12-18 months of age a booster dose of Synflorix vaccine co-administered with Infanrix hexa vaccine. In this study, in the Year 4 (111347 study), subjects had received at Month 48 (4 years post Dose 1 in study 105553) one additional dose of Synflorix vaccine. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix and/or against varicella (a single dose of Varilrix).

| Arm type | Experimental |
|---|---|

| | |
|---|---|
| Investigational medicinal product name | Prevenar |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

3 doses received in primary vaccination study 10PN-PD-DT-001 (1105553)

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

Dosage and administration details:

1 dose in booster study 10PN-PD-DIT-007 (107046); 1 dose during this study at follow-up visit (Visit 3)

| **Number of subjects in period 4[3]** | Synflorix + Infanrix + Havrix and/or Varilrix Group | Prevenar + Infanrix + Havrix and/or Varilrix Group | Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix |
|---|---|---|---|
| Started | 264 | 20 | 65 |
| Completed | 263 | 19 | 64 |
| Not completed | 1 | 1 | 1 |
| Parents' Decision | - | - | 1 |
| Lost to follow-up | 1 | 1 | - |

Notes:

[3] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Out of the 426 subjects who participated to the year 4 persistence analysis in study 111347, 349 participated to the Immunological Memory phase in this study 111347 and 77 were lost to follow up/did not participate to this 2nd phase. Kindly note that to these 349 subjects, 100 additional subjects were added, who constituted an Unprimed Group. No withdrawal was reported for this group, which included 53 females and 47 males and in which mean age was 65.4 months (SD: 1.31 months).

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Synflorix + Infanrix + Havrix and/or Varilrix Group |
| Reporting group description: | |
| This group consisted of subjects primed with Synflorix vaccine in the 10PN-PD-DIT-001 (1105553) and 007 (107046) studies. In 105553 study, subjects had been primed with 3 doses of Synflorix vaccine at 2, 3 and 4 months of age co-administered with Infanrix related vaccines. In 107046 study, subjects had received a booster dose of Synflorix vaccine at 12-18 months of age co-administered with Infanrix hexa vaccine. In this study, in the Year 4 (111347 study), subjects received at Month 48 (4 years post Dose 1 in study 105553) one additional dose of Synflorix vaccine. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix) and/or against varicella (a single dose of Varilrix). | |
| Reporting group title | Prevenar + Infanrix + Havrix and/or Varilrix Group |
| Reporting group description: | |
| This group consisted of subjects vaccinated with Prevenar vaccine in the 10PN-PD-DIT-001 (105553) and 007 (107046) studies. In 105553 study, subjects had been primed with 3 doses of Prevenar vaccine at 2, 3 and 4 months of age co-administered with Infanrix related vaccines. In 107046 study, subjects had received a booster dose at 12-18 months of age of Prevenar vaccine co-administered with Infanrix hexa vaccine. In this study, in the Year 4 111347 study, subjects had received at Month 48 (4 years post Dose 1 in study 105553) one dose of Synflorix vaccine. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix and/or against varicella (a single dose of Varilrix). | |
| Reporting group title | Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix |
| Reporting group description: | |
| This group consisted of subjects vaccinated with Prevenar and Synflorix vaccines in the 10PN-PD-DIT-001 (105553) and 10PN-PD-DIT-007 (107046) studies. In 105553 study, subjects had been primed with 3 doses Prevenar vaccine at 2, 3 and 4 months of age co-administered with Infanrix related vaccines. In the 107046 study, subjects had received at 12-18 months of age a booster dose of Synflorix vaccine co-administered with Infanrix hexa vaccine. In this study, in the Year 4 (111347 study), subjects had received at Month 48 (4 years post Dose 1 in study 105553) one additional dose of Synflorix vaccine. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix and/or against varicella (a single dose of Varilrix). | |

| **Reporting group values** | Synflorix + Infanrix + Havrix and/or Varilrix Group | Prevenar + Infanrix + Havrix and/or Varilrix Group | Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix |
|---|---|---|---|
| Number of subjects | 391 | 31 | 102 |
| Age categorical<br>Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 391 | 31 | 102 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 0 | 0 | 0 |
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |
| Age Continuous | | | |
| Data was presented for Follow-up Period: Year 1 | | | |
| Units: Months | | | |
| arithmetic mean | 29.1 | 29.0 | 29.1 |
| standard deviation | ± 0.88 | ± 0.75 | ± 0.81 |

| | | | |
|---|---|---|---|
| Sex: Female, Male | | | |
| Data was presented for Follow-up Period Year 1 | | | |
| Units: Participants | | | |
| Female | 203 | 14 | 52 |
| Male | 188 | 17 | 50 |
| Race/Ethnicity, Customized | | | |
| Data was presented for Follow-up Period: Year 1 | | | |
| Units: Subjects | | | |
| White - caucasia/ european heritage | 386 | 31 | 102 |
| White arabic/ north african heritage | 4 | 0 | 0 |
| Other, not specified | 1 | 0 | 0 |
| Asian - Central/South Asian heritage | 0 | 0 | 0 |

| **Reporting group values** | Total | | |
|---|---|---|---|
| Number of subjects | 524 | | |
| 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) | 524 | | |
| Adolescents (12-17 years) | 0 | | |
| Adults (18-64 years) | 0 | | |
| From 65-84 years | 0 | | |
| 85 years and over | 0 | | |
| Age Continuous | | | |
| Data was presented for Follow-up Period: Year 1 | | | |
| Units: Months | | | |
| arithmetic mean | | | |
| standard deviation | - | | |
| Sex: Female, Male | | | |
| Data was presented for Follow-up Period Year 1 | | | |
| Units: Participants | | | |
| Female | 269 | | |
| Male | 255 | | |
| Race/Ethnicity, Customized | | | |
| Data was presented for Follow-up Period: Year 1 | | | |
| Units: Subjects | | | |
| White - caucasia/ european heritage | 519 | | |
| White arabic/ north african heritage | 4 | | |
| Other, not specified | 1 | | |
| Asian - Central/South Asian heritage | 0 | | |

## Subject analysis sets

| | |
|---|---|
| Subject analysis set title | Unprimed Group |
| Subject analysis set type | Per protocol |

Subject analysis set description:

This group consisted of subjects between, and including, 64-68 months of age at the time of additional vaccination (primed subjects) or dose 1 (unprimed subjects), and for whom the investigator believed that their parents/guardians could and would comply with the requirements of the protocol. Subjects were not previously vaccinated with any pneumococcal vaccine and received 2 doses of Synflorix vaccine at 64-68 and 66-70 months of age (at Day 0 and Month 2). The Unprimed Group was added only in Year 4 of the study.

| **Reporting group values** | Unprimed Group | | |
|---|---|---|---|
| Number of subjects | 100 | | |
| Age categorical<br>Units: Subjects | | | |
| In utero | 0 | | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | | |
| Newborns (0-27 days) | 0 | | |
| Infants and toddlers (28 days-23 months) | 0 | | |
| Children (2-11 years) | 100 | | |
| Adolescents (12-17 years) | 0 | | |
| Adults (18-64 years) | 0 | | |
| From 65-84 years | 0 | | |
| 85 years and over | 0 | | |
| Age Continuous | | | |
| Data was presented for Follow-up Period: Year 1 | | | |
| Units: Months | | | |
| arithmetic mean | 65.4 | | |
| standard deviation | ± 1.31 | | |
| Sex: Female, Male | | | |
| Data was presented for Follow-up Period Year 1 | | | |
| Units: Participants | | | |
| Female | 53 | | |
| Male | 47 | | |
| Race/Ethnicity, Customized | | | |
| Data was presented for Follow-up Period: Year 1 | | | |
| Units: Subjects | | | |
| White - caucasia/ european heritage | 98 | | |
| White arabic/ north african heritage | 1 | | |
| Other, not specified | 1 | | |
| Asian - Central/South Asian heritage | 1 | | |

### End points reporting groups

| Reporting group title | Synflorix + Infanrix + Havrix and/or Varilrix Group |
|---|---|

Reporting group description:

This group consisted of subjects primed with Synflorix vaccine in the 10PN-PD-DIT-001 (1105553) and 007 (107046) studies. In 105553 study, subjects had been primed with 3 doses of Synflorix vaccine at 2, 3 and 4 months of age co-administered with Infanrix related vaccines. In 107046 study, subjects had received a booster dose of Synflorix vaccine at 12-18 months of age co-administered with Infanrix hexa vaccine. In this study, in the Year 4 (111347 study), subjects received at Month 48 (4 years post Dose 1 in study 105553) one additional dose of Synflorix vaccine. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix) and/or against varicella (a single dose of Varilrix).

| Reporting group title | Prevenar + Infanrix + Havrix and/or Varilrix Group |
|---|---|

Reporting group description:

This group consisted of subjects vaccinated with Prevenar vaccine in the 10PN-PD-DIT-001 (105553) and 007 (107046) studies. In 105553 study, subjects had been primed with 3 doses of Prevenar vaccine at 2, 3 and 4 months of age co-administered with Infanrix related vaccines. In 107046 study, subjects had received a booster dose at 12-18 months of age of Prevenar vaccine co-administered with Infanrix hexa vaccine. In this study, in the Year 4 111347 study, subjects had received at Month 48 (4 years post Dose 1 in study 105553) one dose of Synflorix vaccine. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix and/or against varicella (a single dose of Varilrix).

| Reporting group title | Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix |
|---|---|

Reporting group description:

This group consisted of subjects vaccinated with Prevenar and Synflorix vaccines in the 10PN-PD-DIT-001 (105553) and 10PN-PD-DIT-007 (107046) studies. In 105553 study, subjects had been primed with 3 doses Prevenar vaccine at 2, 3 and 4 months of age co-administered with Infanrix related vaccines. In the 107046 study, subjects had received at 12-18 months of age a booster dose of Synflorix vaccine co-administered with Infanrix hexa vaccine. In this study, in the Year 4 (111347 study), subjects had received at Month 48 (4 years post Dose 1 in study 105553) one additional dose of Synflorix vaccine. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix and/or against varicella (a single dose of Varilrix).

| Reporting group title | Synflorix + Infanrix + Havrix and/or Varilrix Group |
|---|---|

Reporting group description:

This group consisted of subjects primed with Synflorix vaccine in the 10PN-PD-DIT-001 (1105553) and 007 (107046) studies. In 105553 study, subjects had been primed with 3 doses of Synflorix vaccine at 2, 3 and 4 months of age co-administered with Infanrix related vaccines. In 107046 study, subjects had received a booster dose of Synflorix vaccine at 12-18 months of age co-administered with Infanrix hexa vaccine. In this study, in the Year 4 (111347 study), subjects received at Month 48 (4 years post Dose 1 in study 105553) one additional dose of Synflorix vaccine. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix) and/or against varicella (a single dose of Varilrix).

| Reporting group title | Prevenar + Infanrix + Havrix and/or Varilrix Group |
|---|---|

Reporting group description:

This group consisted of subjects vaccinated with Prevenar vaccine in the 10PN-PD-DIT-001 (105553) and 007 (107046) studies. In 105553 study, subjects had been primed with 3 doses of Prevenar vaccine at 2, 3 and 4 months of age co-administered with Infanrix related vaccines. In 107046 study, subjects had received a booster dose at 12-18 months of age of Prevenar vaccine co-administered with Infanrix hexa vaccine. In this study, in the Year 4 111347 study, subjects had received at Month 48 (4 years post Dose 1 in study 105553) one dose of Synflorix vaccine. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix and/or against varicella (a single dose of Varilrix).

| Reporting group title | Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix |
|---|---|

Reporting group description:

This group consisted of subjects vaccinated with Prevenar and Synflorix vaccines in the 10PN-PD-DIT-001 (105553) and 10PN-PD-DIT-007 (107046) studies. In 105553 study, subjects had been primed with 3 doses Prevenar vaccine at 2, 3 and 4 months of age co-administered with Infanrix related vaccines. In the 107046 study, subjects had received at 12-18 months of age a booster dose of Synflorix vaccine co-administered with Infanrix hexa vaccine. In this study, in the Year 4 (111347 study), subjects had received at Month 48 (4 years post Dose 1 in study 105553) one additional dose of Synflorix vaccine. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix and/or against varicella (a single dose of Varilrix).

| Reporting group title | Synflorix + Infanrix + Havrix and/or Varilrix Group |
|---|---|

Reporting group description:

This group consisted of subjects primed with Synflorix vaccine in the 10PN-PD-DIT-001 (1105553) and 007 (107046) studies. In 105553 study, subjects had been primed with 3 doses of Synflorix vaccine at 2, 3 and 4 months of age co-administered with Infanrix related vaccines. In 107046 study, subjects had received a booster dose of Synflorix vaccine at 12-18 months of age co-administered with Infanrix hexa vaccine. In this study, in the Year 4 (111347 study), subjects received at Month 48 (4 years post Dose 1 in study 105553) one additional dose of Synflorix vaccine. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix) and/or against varicella (a single dose of Varilrix).

| Reporting group title | Prevenar + Infanrix + Havrix and/or Varilrix Group |
|---|---|

Reporting group description:

This group consisted of subjects vaccinated with Prevenar vaccine in the 10PN-PD-DIT-001 (105553) and 007 (107046) studies. In 105553 study, subjects had been primed with 3 doses of Prevenar vaccine at 2, 3 and 4 months of age co-administered with Infanrix related vaccines. In 107046 study, subjects had received a booster dose at 12-18 months of age of Prevenar vaccine co-administered with Infanrix hexa vaccine. In this study, in the Year 4 111347 study, subjects had received at Month 48 (4 years post Dose 1 in study 105553) one dose of Synflorix vaccine. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix and/or against varicella (a single dose of Varilrix).

| Reporting group title | Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix |
|---|---|

Reporting group description:

This group consisted of subjects vaccinated with Prevenar and Synflorix vaccines in the 10PN-PD-DIT-001 (105553) and 10PN-PD-DIT-007 (107046) studies. In 105553 study, subjects had been primed with 3 doses Prevenar vaccine at 2, 3 and 4 months of age co-administered with Infanrix related vaccines. In the 107046 study, subjects had received at 12-18 months of age a booster dose of Synflorix vaccine co-administered with Infanrix hexa vaccine. In this study, in the Year 4 (111347 study), subjects had received at Month 48 (4 years post Dose 1 in study 105553) one additional dose of Synflorix vaccine. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix and/or against varicella (a single dose of Varilrix).

| Reporting group title | Synflorix + Infanrix + Havrix and/or Varilrix Group |
|---|---|

Reporting group description:

This group consisted of subjects primed with Synflorix vaccine in the 10PN-PD-DIT-001 (1105553) and 007 (107046) studies. In 105553 study, subjects had been primed with 3 doses of Synflorix vaccine at 2, 3 and 4 months of age co-administered with Infanrix related vaccines. In 107046 study, subjects had received a booster dose of Synflorix vaccine at 12-18 months of age co-administered with Infanrix hexa vaccine. In this study, in the Year 4 (111347 study), subjects received at Month 48 (4 years post Dose 1 in study 105553) one additional dose of Synflorix vaccine. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix) and/or against varicella (a single dose of Varilrix).

| Reporting group title | Prevenar + Infanrix + Havrix and/or Varilrix Group |
|---|---|

Reporting group description:

This group consisted of subjects vaccinated with Prevenar vaccine in the 10PN-PD-DIT-001 (105553) and 007 (107046) studies. In 105553 study, subjects had been primed with 3 doses of Prevenar vaccine at 2, 3 and 4 months of age co-administered with Infanrix related vaccines. In 107046 study, subjects had received a booster dose at 12-18 months of age of Prevenar vaccine co-administered with Infanrix hexa vaccine. In this study, in the Year 4 111347 study, subjects had received at Month 48 (4 years post Dose 1 in study 105553) one dose of Synflorix vaccine. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix and/or against varicella (a single dose of Varilrix).

| Reporting group title | Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix |
|---|---|

Reporting group description:

This group consisted of subjects vaccinated with Prevenar and Synflorix vaccines in the 10PN-PD-DIT-001 (105553) and 10PN-PD-DIT-007 (107046) studies. In 105553 study, subjects had been primed with 3 doses Prevenar vaccine at 2, 3 and 4 months of age co-administered with Infanrix related vaccines. In the 107046 study, subjects had received at 12-18 months of age a booster dose of Synflorix vaccine co-administered with Infanrix hexa vaccine. In this study, in the Year 4 (111347 study), subjects had received at Month 48 (4 years post Dose 1 in study 105553) one additional dose of Synflorix vaccine. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix and/or against varicella (a single dose of Varilrix).

| Subject analysis set title | Unprimed Group |
|---|---|
| Subject analysis set type | Per protocol |

Subject analysis set description:

This group consisted of subjects between, and including, 64-68 months of age at the time of additional vaccination (primed subjects) or dose 1 (unprimed subjects), and for whom the investigator believed that their parents/guardians could and would comply with the requirements of the protocol. Subjects were not previously vaccinated with any pneumococcal vaccine and received 2 doses of Synflorix vaccine at 64-68 and 66-70 months of age (at Day 0 and Month 2). The Unprimed Group was added only in Year 4 of the study.

## Primary: Number of subjects with anti-vaccine pneumococcal serotypes antibody concentrations greater than or equal to (≥) the cut-off [Follow-up Period: Persistence Analysis in Year 1 (111345 sub-study)]

| End point title | Number of subjects with anti-vaccine pneumococcal serotypes antibody concentrations greater than or equal to (≥) the cut-off [Follow-up Period: Persistence Analysis in Year 1 (111345 sub-study)][1] |
|---|---|

End point description:

A seropositive subject was a subject whose antibody concentration was greater than or equal to (≥) the cut-off value. Analysis was performed using the 22F-inhibition Enzyme-linked immunosorbent assay (ELISA), using 0.05 microgram per milliliter (µg/mL) as seropositivity cut off.

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

End point timeframe:

At Year 1 (Y1) (post booster vaccination administered in study 10PN-PD-DIT-007)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

| **End point values** | Synflorix + Infanrix + Havrix and/or Varilrix Group | Prevenar + Infanrix + Havrix and/or Varilrix Group | Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 389 | 31 | 102 | |
| Units: Participants | | | | |
| Anti-1 antibodies, Y1 (N= 387, 29, 102) | 372 | 7 | 99 | |
| Anti-4 antibodies, Y1 (N= 387, 31, 102) | 384 | 31 | 102 | |
| Anti-5 antibodies, Y1 (N= 387, 30, 101) | 386 | 19 | 101 | |
| Anti-6B antibodies, Y1 (N= 389, 31, 102) | 384 | 31 | 100 | |
| Anti-7F antibodies, Y1 (N= 387, 31, 102) | 387 | 17 | 102 | |
| Anti-9V antibodies, Y1 (N= 388, 31, 102) | 388 | 17 | 102 | |
| Anti-14 antibodies, Y1 (N= 388, 31, 102) | 387 | 31 | 102 | |
| Anti-18C antibodies, Y1 (N= 384, 31, 102) | 384 | 31 | 102 | |
| Anti-19F antibodies, Y1 (N= 387, 31, 102) | 387 | 31 | 102 | |
| Anti-23F antibodies, Y1 (N= 388, 31, 102) | 386 | 31 | 102 | |

### Statistical analyses

No statistical analyses for this end point

## Primary: Number of subjects with anti-vaccine pneumococcal serotypes antibody concentrations ≥ the cut-off [Follow-up Period: Persistence Analysis in Year 2 (111346 sub-study)]

| End point title | Number of subjects with anti-vaccine pneumococcal serotypes antibody concentrations ≥ the cut-off [Follow-up Period: Persistence Analysis in Year 2 (111346 sub-study)][2] |
|---|---|

End point description:

A seropositive subject was a subject whose antibody concentration was greater than or equal to (≥) the cut-off value. Analysis was performed using the 22F-inhibition Enzyme -linked immunosorbent assay (ELISA), using 0.05 µg/mL as seropositivity cut off.

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

End point timeframe:

At Year 2 (Y2) (post booster vaccination administered in study 10PN-PD-DIT-007)

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

| **End point values** | Synflorix + Infanrix + Havrix and/or Varilrix Group | Prevenar + Infanrix + Havrix and/or Varilrix Group | Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 368 | 30 | 96 | |
| Units: Participants | | | | |
| Anti-1 antibodies, Y2 (N= 367, 29, 96) | 354 | 18 | 90 | |
| Anti-4 antibodies, Y2 (N= 368, 30, 96) | 356 | 30 | 96 | |
| Anti-5 antibodies, Y2 (N= 368, 29, 95) | 362 | 21 | 95 | |
| Anti-6B antibodies, Y2 (N= 368, 30, 96) | 355 | 30 | 95 | |
| Anti-7F antibodies, Y2 (N= 368, 30, 96) | 367 | 19 | 95 | |
| Anti-9V antibodies, Y2 (N= 368, 30, 96) | 362 | 30 | 96 | |
| Anti-14 antibodies, Y2 (N= 368, 30, 96) | 367 | 30 | 96 | |
| Anti-18C antibodies, Y2 (N= 368, 30, 96) | 365 | 30 | 96 | |
| Anti-19F antibodies, Y2 (N= 368, 30, 95) | 368 | 30 | 95 | |
| Anti-23F antibodies, Y2 (N= 368, 30, 96) | 357 | 30 | 95 | |

## Statistical analyses

No statistical analyses for this end point

## Primary: Number of subjects with anti-vaccine pneumococcal serotypes antibody concentrations ≥ the cut-off [Follow-up Period: Persistence Analysis in Year 4 (111347 sub-study)]

| End point title | Number of subjects with anti-vaccine pneumococcal serotypes antibody concentrations ≥ the cut-off [Follow-up Period: Persistence Analysis in Year 4 (111347 sub-study)][3] |
|---|---|

End point description:

A seropositive subject was a subject whose antibody concentration was greater than or equal to (≥) the cut-off value. Analysis was performed using the 22F-inhibition Enzyme-linked immunosorbent assay (ELISA), using 0.05 µg/mL as seropositivity cut off.

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

End point timeframe:

At Year 4 (Y4) (post booster vaccination administered in study 10PN-PD-DIT-007)

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

| **End point values** | Synflorix + Infanrix + Havrix and/or Varilrix Group | Prevenar + Infanrix + Havrix and/or Varilrix Group | Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 264 | 19 | 75 | |
| Units: Participants | | | | |
| Anti-1 antibodies, Y4 (N= 263, 19, 75) | 238 | 14 | 75 | |
| Anti-4 antibodies, Y4 (N= 263, 18, 74) | 238 | 18 | 74 | |
| Anti-5 antibodies, Y4 (N= 263, 19, 74) | 257 | 19 | 73 | |
| Anti-6B antibodies, Y4 (N= 263, 19, 75) | 258 | 19 | 74 | |
| Anti-7F antibodies, Y4 (N= 263, 19,75) | 260 | 13 | 73 | |
| Anti-9V antibodies, Y4 (N= 263, 19, 75) | 255 | 19 | 75 | |
| Anti-14 antibodies, Y4 (N= 263, 19, 75) | 2633 | 19 | 75 | |
| Anti-18C antibodies, Y4 (N= 263, 19, 74) | 256 | 19 | 73 | |
| Anti-19F antibodies, Y4 (N= 263, 19, 75) | 260 | 19 | 75 | |
| Anti-23F antibodies, Y4 (N= 262, 19, 75) | 254 | 19 | 74 | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Antibody concentrations against pneumococcal serotypes [Follow-Up Period: Persistence Analysis in Year 1 (111345 sub-study)]

| End point title | Antibody concentrations against pneumococcal serotypes [Follow-Up Period: Persistence Analysis in Year 1 (111345 sub-study)] |
|---|---|

End point description:

Pneumococcal serotypes assessed were 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F. Antibody concentrations against pneumococcal serotypes were determined as Geometric Mean Antibody Concentrations (GMC) and expressed as micro grams per milliliter (µg/mL).The seropositivity cut-off for the assay was ≥ 0.05 µg/mL.

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

End point timeframe:

At Year 1 (Y1) (post booster vaccination administered in study 10PN-PD-DIT-007)

| End point values | Synflorix + Infanrix + Havrix and/or Varilrix Group | Prevenar + Infanrix + Havrix and/or Varilrix Group | Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 389 | 31 | 102 | |
| Units: µg/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-1 antibodies, Y1 (N= 387, 29, 102) | 0.29 (0.27 to 0.32) | 0.04 (0.03 to 0.06) | 0.26 (0.21 to 0.31) | |
| Anti-4 antibodies, Y1 (N= 387, 31, 102) | 0.5 (0.45 to 0.55) | 0.59 (0.46 to 0.75) | 1.01 (0.84 to 1.21) | |
| Anti-5 antibodies, Y1 (N= 387, 30, 101) | 0.59 (0.54 to 0.65) | 0.07 (0.05 to 0.11) | 0.42 (0.35 to 0.52) | |
| Anti-6B antibodies, Y1 (N= 389, 31, 102) | 0.52 (0.45 to 0.6) | 0.98 (0.63 to 1.53) | 0.54 (0.42 to 0.69) | |
| Anti-7F antibodies, Y1 (N= 387, 31, 102) | 0.71 (0.66 to 0.77) | 0.08 (0.05 to 0.13) | 0.83 (0.7 to 0.99) | |
| Anti-9V antibodies, Y1 (N= 388, 31, 102) | 0.79 (0.71 to 0.89) | 0.93 (0.7 to 1.22) | 0.58 (0.49 to 0.68) | |
| Anti-14 antibodies, Y1 (N= 388, 31, 102) | 1.27 (1.12 to 1.44) | 1.79 (1.29 to 2.48) | 1.47 (1.17 to 1.85) | |
| Anti-18C antibodies, Y1 (N= 384, 31, 102) | 0.88 (0.81 to 0.96) | 0.91 (0.71 to 1.16) | 0.82 (0.69 to 0.98) | |
| Anti-19F antibodies, Y1 (N= 387, 31, 102) | 1.43 (1.27 to 1.6) | 0.83 (0.47 to 1.45) | 1.51 (1.19 to 1.92) | |
| Anti-23F antibodies, Y1 (N= 388, 30, 102) | 0.61 (0.54 to 0.69) | 1.18 (0.84 to 1.68) | 0.7 (0.56 to 0.88) | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Antibody concentrations against pneumococcal serotypes [Follow-Up Period: Persistence Analysis in Year 2 (111346 sub-study)]

| End point title | Antibody concentrations against pneumococcal serotypes [Follow-Up Period: Persistence Analysis in Year 2 (111346 sub-study)] |
|---|---|

End point description:

Pneumococcal serotypes assessed were 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F. Antibody concentrations against pneumococcal serotypes were determined as Geometric Mean Antibody Concentrations (GMC) and expressed as micro grams per milliliter (µg/mL). The seropositivity cut-off for the assay was ≥ 0.05 µg/mL.

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

End point timeframe:

At Year 2 (Y2) (post booster vaccination administered in study 10PN-PD-DIT-007)

| End point values | Synflorix + Infanrix + Havrix and/or Varilrix Group | Prevenar + Infanrix + Havrix and/or Varilrix Group | Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 368 | 30 | 96 | |
| Units: µg/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-1 antibodies, Y2 (N= 367, 29, 96) | 0.19 (0.17 to 0.21) | 0.07 (0.05 to 0.10) | 0.17 (0.14 to 0.20) | |
| Anti-4 antibodies, Y2 (N= 368, 30, 96) | 0.27 (0.24 to 0.3) | 0.3 (0.24 to 0.38) | 0.52 (0.43 to 0.64) | |
| Anti-5 antibodies, Y2 (N= 368, 29, 95) | 0.41 (0.37 to 0.45) | 0.09 (0.06 to 0.13) | 0.33 (0.27 to 0.41) | |
| Anti-6B antibodies, Y2 (N= 368, 30, 96) | 0.70 (0.58 to 0.83) | 0.99 (0.57 to 1.71) | 0.9 (0.63 to 1.29) | |
| Anti-7F antibodies, Y2 (N= 368, 30, 96) | 0.53 (0.48 to 0.58) | 0.1 (0.06 to 0.16) | 0.59 (0.49 to 0.71) | |
| Anti-9V antibodies, Y2 (N= 368, 30, 96) | 0.64 (0.54 to 0.75) | 0.61 (0.37 to 1) | 0.5 (0.37 to 0.68) | |
| Anti-14 antibodies, Y2 (N= 368, 30, 96) | 1.73 (1.48 to 2.02) | 1.94 (1.12 to 3.36) | 1.7 (1.25 to 2.31) | |
| Anti-18C antibodies, Y2 (N= 368, 30, 96) | 0.54 (0.48 to 0.62) | 0.59 (0.39 to 0.88) | 0.48 (0.38 to 0.59) | |
| Anti-19F antibodies, Y2 (N= 368, 30, 95) | 2.16 (1.77 to 2.65) | 0.99 (0.51 to 1.91) | 2.41 (1.67 to 3.46) | |
| Anti-23F antibodies, Y2 (N= 368, 30, 96) | 0.68 (0.56 to 0.82) | 1.24 (0.83 to 1.85) | 0.64 (0.48 to 0.86) | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Antibody concentrations against pneumococcal serotypes [Follow-up Period: Persistence Analysis in Year 4 (111347 sub-study)]

| End point title | Antibody concentrations against pneumococcal serotypes [Follow-up Period: Persistence Analysis in Year 4 (111347 sub-study)] |
|---|---|

End point description:

Pneumococcal serotypes assessed were serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F. Antibody concentrations against pneumococcal serotypes were determined as Geometric Mean Antibody Concentrations (GMC) and expressed as micro grams per milliliter (µg/mL). The seropositivity cut-off for the assay was ≥ 0.05 µg/mL.

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

End point timeframe:

At Year 4 (Y4) (post booster vaccination administered in study 10PN-PDDIT- 007)

| End point values | Synflorix + Infanrix + Havrix and/or Varilrix Group | Prevenar + Infanrix + Havrix and/or Varilrix Group | Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 264 | 19 | 75 | |
| Units: µg/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-1 antibodies, Y4 (N= 263, 19, 75) | 0.2 (0.17 to 0.24) | 0.17 (0.07 to 0.43) | 0.23 (0.17 to 0.32) | |
| Anti-4 antibodies, Y4 (N= 263, 19, 74) | 0.19 (0.16 to 0.22) | 0.23 (0.12 to 0.41) | 0.31 (0.25 to 0.38) | |
| Anti-5 antibodies, Y4 (N= 263, 19, 74) | 0.36 (0.31 to 0.4) | 0.19 (0.1 to 0.35) | 0.35 (0.28 to 0.43) | |
| Anti-6B antibodies, Y4 (N= 263, 19, 75) | 1.3 (1.1 to 1.55) | 1.19 (0.68 to 2.07) | 0.97 (0.74 to 1.27) | |
| Anti-7F antibodies, Y4 (N= 263, 19, 75) | 0.44 (0.38 to 0.52) | 0.16 (0.08 to 0.36) | 0.49 (0.37 to 0.65) | |
| Anti-9V antibodies, Y4 (N= 263, 19, 75) | 1.17 (0.92 to 1.47) | 1.19 (0.43 to 3.27) | 0.67 (0.46 to 0.99) | |
| Anti-14 antibodies, Y4 (N= 263, 19, 75) | 3.66 (3.01 to 4.45) | 2.57 (1.22 to 5.42) | 2.94 (2.11 to 4.12) | |
| Anti-18C antibodies, Y4 (N= 263, 19, 74) | 0.7 (0.58 to 0.84) | 0.87 (0.4 to 1.88) | 0.63 (0.45 to 0.89) | |
| Anti-19F antibodies, Y4 (N= 263, 19, 75) | 4.17 (3.4 to 5.1) | 4.74 (2.24 to 10) | 4.05 (3.03 to 5.41) | |
| Anti-23F antibodies, Y4 (N= 262, 19, 75) | 1.57 (1.26 to 1.96) | 1.64 (1.15 to 2.34) | 1.12 (0.79 to 1.58) | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Antibody concentrations against pneumococcal serotypes [Follow-up Period: Immunogenicity Analysis in Year 4 (111347 sub-study)]

| End point title | Antibody concentrations against pneumococcal serotypes [Follow-up Period: Immunogenicity Analysis in Year 4 (111347 sub-study)] |
|---|---|

End point description:

Anti-pneumococcal serotypes assessed were serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F . Antibody concentrations against pneumococcal serotypes were determined as Geometric Mean Antibody Concentrations (GMC) and expressed as micro grams per milliliter (µg/mL). The seropositivity cut-off for the assay was ≥ 0.05 µg/mL.

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

End point timeframe:

For primed groups: At Month 48+7 days after additional dose (D7);For unprimed group: at Day 0 (D0) (Pre-vaccination [PRE]), at Day 7 (D7) post dose 1 (of the 2-dose catch-up vaccination) and at Month 3 (M3) post dose 2 (of the 2-dose catch-up vaccination)

| End point values | Synflorix + Infanrix + Havrix and/or Varilrix Group | Prevenar + Infanrix + Havrix and/or Varilrix Group | Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix | Unprimed Group |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 210 | 14 | 55 | 98 |
| Units: µg/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-1 antibodies, PRE (N=0, 0, 0, 97) | 0 (0 to 0) | 0 (0 to 0) | 0 (0 to 0) | 0.1 (0.08 to 0.13) |
| Anti-1 antibodies, D7 (N= 208, 14, 54, 98) | 5.36 (4.54 to 6.33) | 3.04 (1.22 to 7.56) | 5 (3.72 to 6.71) | 1.35 (1.08 to 1.69) |
| Anti-1 antibodies, M3 (N=0, 0, 0, 98) | 0 (0 to 0) | 0 (0 to 0) | 0 (0 to 0) | 2.39 (2.06 to 2.78) |
| Anti-4 antibodies, PRE (N= 0, 0, 0, 97) | 0 (0 to 0) | 0 (0 to 0) | 0 (0 to 0) | 0.04 (0.03 to 0.05) |
| Anti-4 antibodies, D7 (N=208, 14, 54, 98) | 12.11 (10.08 to 14.54) | 10.45 (6.49 to 16.81) | 7.13 (5.18 to 9.82) | 4.74 (3.77 to 5.95) |
| Anti-4 antibodies, M3 (N=0, 0, 0, 98) | 0 (0 to 0) | 0 (0 to 0) | 0 (0 to 0) | 7.32 (6.7 to 8) |
| Anti-5 antibodies, PRE (N=0, 0, 0, 97) | 0 (0 to 0) | 0 (0 to 0) | 0 (0 to 0) | 0.1 (0.08 to 0.12) |
| Anti-5 antibodies, D7 (N=208, 14, 54, 98) | 6.23 (5.19 to 7.49) | 3.24 (1.44 to 7.29) | 8.15 (5.71 to 11.63) | 1.2 (0.97 to 1.49) |
| Anti-5 antibodies, M3 (N=0, 0, 0, 98) | 0 (0 to 0) | 0 (0 to 0) | 0 (0 to 0) | 3.1 (2.7 to 3.55) |
| Anti-6B antibodies, PRE (N= 0, 0, 0, 97) | 0 (0 to 0) | 0 (0 to 0) | 0 (0 to 0) | 0.21 (0.15 to 0.29) |
| Anti-6B antibodies, D7 (N= 208, 14, 54, 97) | 3.68 (3.16 to 4.28) | 2.85 (1.89 to 4.3) | 2.15 (1.62 to 2.85) | 0.53 (0.4 to 0.71) |
| Anti-6B antibodies, M3 (N= 0, 0, 0, 98) | 0 (0 to 0) | 0 (0 to 0) | 0 (0 to 0) | 1.25 (1.01 to 1.54) |
| Anti-7F antibodies, PRE (N= 0, 0, 0, 97) | 0 (0 to 0) | 0 (0 to 0) | 0 (0 to 0) | 0.12 (0.09 to 0.16) |
| Anti-7F antibodies, D7 (N=208, 14, 54, 98) | 7.16 (6.11 to 8.39) | 3.26 (1.67 to 6.35) | 7.57 (5.84 to 9.81) | 1.67 (1.33 to 2.09) |
| Anti-7F antibodies, M3 (N= 0, 0, 0, 98) | 0 (0 to 0) | 0 (0 to 0) | 0 (0 to 0) | 4.55 (3.93 to 5.26) |
| Anti-9V antibodies, PRE (N= 0, 0, 0, 97) | 0 (0 to 0) | 0 (0 to 0) | 0 (0 to 0) | 0.19 (0.12 to 0.28) |
| Anti-9V antibodies, D7 (N=208, 14, 54, 98) | 9.94 (8.59 to 11.51) | 9 (5.49 to 14.77) | 5.32 (4.08 to 6.94) | 0.9 (0.66 to 1.23) |
| Anti-9V antibodies, M3 (N= 0, 0, 0, 98) | 0 (0 to 0) | 0 (0 to 0) | 0 (0 to 0) | 2.2 (1.85 to 2.62) |
| Anti-14 antibodies, PRE (N= 0, 0, 0, 96) | 0 (0 to 0) | 0 (0 to 0) | 0 (0 to 0) | 0.58 (0.38 to 0.87) |
| Anti-14 antibodies, D7 (N= 208, 14, 54, 98) | 19.38 (16.74 to 22.43) | 13.26 (6.91 to 25.43) | 18.61 (14.23 to 24.34) | 1.72 (1.2 to 2.46) |
| Anti-14 antibodies, M3 (N= 0, 0, 0, 98) | 0 (0 to 0) | 0 (0 to 0) | 0 (0 to 0) | 7.81 (6.34 to 9.63) |
| Anti-18C antibodies, PRE (N= 0, 0, 0, 96) | 0 (0 to 0) | 0 (0 to 0) | 0 (0 to 0) | 0.1 (0.07 to 0.15) |
| Anti-18C antibodies, D7 (N=208, 14, 54, 98) | 15.51 (13.06 to 18.43) | 19.71 (11.87 to 32.74) | 13.34 (9.34 to 19.05) | 2.26 (1.66 to 3.09) |
| Anti-18C antibodies, M3 (N= 0, 0, 0, 98) | 0 (0 to 0) | 0 (0 to 0) | 0 (0 to 0) | 13.21 (11.44 to 15.25) |
| Anti-19F antibodies, PRE (N= 0, 0, 0, 96) | 0 (0 to 0) | 0 (0 to 0) | 0 (0 to 0) | 0.6 (0.4 to 0.89) |
| Anti-19F antibodies, D7 (N=208, 14, 54, 98) | 11.63 (10 to 13.51) | 16.44 (10.68 to 25.29) | 8.09 (6.29 to 10.42) | 5.12 (3.97 to 6.62) |

| | | | | |
|---|---|---|---|---|
| Anti-19F antibodies, M3 (N= 0, 0, 0, 98) | 0 (0 to 0) | 0 (0 to 0) | 0 (0 to 0) | 15.47 (13.08 to 18.29) |
| Anti-23F antibodies, PRE (N= 0, 0, 0, 97) | 0 (0 to 0) | 0 (0 to 0) | 0 (0 to 0) | 0.1 (0.07 to 0.14) |
| Anti-23F antibodies, D7 (N= 208, 14, 54, 98) | 6.5 (5.61 to 7.53) | 9.34 (5.62 to 15.54) | 4.7 (3.43 to 6.45) | 0.42 (0.3 to 0.59) |
| Anti-23F antibodies, M3 (N= 0, 0, 0, 98) | 0 (0 to 0) | 0 (0 to 0) | 0 (0 to 0) | 1.63 (1.32 to 2.01) |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Opsonophagocytic activity (OPA) titers against pneumococcal serotypes [Follow-Up Period: Persistence Analysis in Year 1 (111345 sub-study)]

| | |
|---|---|
| End point title | Opsonophagocytic activity (OPA) titers against pneumococcal serotypes [Follow-Up Period: Persistence Analysis in Year 1 (111345 sub-study)] |

End point description:

Pneumococcal serotypes assessed were OPA-1, OPA-4, OPA-5, OPA-6B, OPA-7F, OPA-9V, OPA-14, OPA-18C, OPA-19F and OPA-23F. The seropositivity cut-off for the assay was ≥ 8. Opsonophagocytic activity was expressed as Geometric Mean Antibody Titers (GMT).

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

End point timeframe:

At Year 1 (Y1) (post booster vaccination administered in study 10PN-PD-DIT-007)

| End point values | Synflorix + Infanrix + Havrix and/or Varilrix Group | Prevenar + Infanrix + Havrix and/or Varilrix Group | Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 359 | 27 | 94 | |
| Units: Titer | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-1 OPA Titers, Y1 (N=354, 27, 92) | 16.2 (13.8 to 19) | 4.8 (3.6 to 6.4) | 7.3 (5.9 to 9) | |
| Anti-4 OPA Titers, Y1 (N= 340, 26, 86) | 59.8 (45.7 to 78.3) | 192.9 (82.4 to 452) | 88.9 (54.6 to 144.6) | |
| Anti-5 OPA Titers, Y1 (N=335, 27, 89) | 24.2 (20.8 to 28.2) | 5.1 (3.6 to 7.4) | 11.2 (8.7 to 14.3) | |
| Anti-6B OPA Titers, Y1 (N=354, 25, 88) | 35.5 (26.5 to 47.5) | 476.9 (175.3 to 1298) | 44.7 (24 to 83.3) | |
| Anti-7F OPA Titers, Y1 (N= 346, 25, 89) | 1855.7 (1644.4 to 2094.1) | 350.4 (121.8 to 1008) | 1617.2 (1152.9 to 2268.3) | |
| Anti-9V OPA Titers, Y1 (N=352, 26, 94) | 791.5 (701.8 to 892.8) | 1240.7 (829.4 to 1855.9) | 370.5 (281.8 to 487.2) | |
| Anti-14 OPA Titers, Y1 (N= 343, 25, 91) | 551.9 (486.5 to 626.2) | 607.3 (385.3 to 957.1) | 456.6 (361.1 to 577.3) | |
| Anti-18C OPA Titers, Y1 (N= 319, 24, 84) | 23.5 (18.6 to 29.8) | 15.5 (6.1 to 39.2) | 10.4 (7.1 to 15.4) | |

| | | | | |
|---|---|---|---|---|
| Anti-19F OPA Titers, Y1 (N= 359, 27, 94) | 53.4 (44.7 to 63.9) | 35.4 (15.9 to 78.6) | 58 (41.6 to 80.7) | |
| Anti-23F OPA Titers, Y1 (N= 336, 27, 93) | 784.9 (625.4 to 985) | 3013.1 (1349.5 to 6727.2) | 552.3 (362.1 to 842.5) | |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Opsonophagocytic activity (OPA) titers against pneumococcal serotypes [Follow-Up Period: Persistence Analysis in Year 2 (111346 sub-study)]**

| | |
|---|---|
| End point title | Opsonophagocytic activity (OPA) titers against pneumococcal serotypes [Follow-Up Period: Persistence Analysis in Year 2 (111346 sub-study)] |

End point description:

Pneumococcal serotypes assessed were OPA-1, OPA-4, OPA-5, OPA-6B, OPA-7F, OPA-9V, OPA-14, OPA-18C, OPA-19F and OPA-23F. The seropositivity cut-off for the assay was ≥ 8. Opsonophagocytic activity was expressed as Geometric Mean Antibody Titers (GMT).

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

End point timeframe:

At Year 2 (Y2) (post booster vaccination administrated in study 10PN-PD-DIT-007)

| **End point values** | Synflorix + Infanrix + Havrix and/or Varilrix Group | Prevenar + Infanrix + Havrix and/or Varilrix Group | Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 354 | 27 | 92 | |
| Units: Titer | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-1 OPA Titers, Y2 (N= 354, 27, 92) | 8.4 (7.3 to 9.7) | 4 (4 to 4) | 6.3 (4.9 to 8) | |
| Anti-4 OPA Titers, Y2 (N= 335, 27, 84) | 29 (22.1 to 38) | 33.5 (11.9 to 94.6) | 39.3 (23.7 to 65.2) | |
| Anti-5 OPA Titers, Y2 (N= 351, 27, 91) | 11.4 (10 to 13) | 4.3 (3.9 to 4.7) | 7.4 (6 to 9.1) | |
| Anti-6B OPA Titers, Y2 (N= 342, 27, 88) | 167.2 (124.1 to 225.2) | 526.1 (210.5 to 1314.4) | 213.7 (117.8 to 387.6) | |
| Anti-7F OPA Titers, Y2 (N= 350, 27, 91) | 1488.7 (1358.3 to 1631.6) | 1068.3 (619.5 to 1842.4) | 1387.8 (1096.2 to 1756.9) | |
| Anti-9V OPA Titers, Y2 (N= 349, 27, 92) | 648.5 (570 to 737.7) | 730.4 (457.7 to 1165.7) | 391 (279.2 to 547.5) | |
| Anti-14 OPA Titers, Y2 (N= 341, 25, 90) | 660.2 (567.2 to 768.4) | 651 (348.6 to 1215.5) | 391 (279.2 to 547.5) | |
| Anti-18C OPA Titers, Y2 (N= 325, 27, 83) | 34.9 (26.6 to 45.7) | 34.8 (11.7 to 103.2) | 17.7 (10.7 to 29.2) | |
| Anti-19F OPA Titers, Y2 (N= 349, 27, 92) | 78.1 (60.9 to 100.2) | 49.2 (21.2 to 113.9) | 105.4 (65.8 to 168.7) | |
| Anti-23F OPA Titers, Y2 (N= 342, 26, 91) | 632 (483 to 827) | 1923 (952.2 to 3883.7) | 435 (250.5 to 755.5) | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Opsonophagocytic activity (OPA) titers against pneumococcal serotypes [Follow-up Period: Persistence Analysis in Year 4 (111347 sub-study)]

| End point title | Opsonophagocytic activity (OPA) titers against pneumococcal serotypes [Follow-up Period: Persistence Analysis in Year 4 (111347 sub-study)] |
|---|---|

End point description:

Pneumococcal serotypes assessed were pneumococcal serotypes OPA-1, OPA-4, OPA-5, OPA-6B, OPA-7F, OPA-9V, OPA-14, OPA-18C, OPA-19F and OPA-23F. The seropositivity cut-off for the assay was ≥ 8. Opsonophagocytic activity was expressed as Geometric Mean Antibody Titers (GMT).

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

End point timeframe:

At Year 4 (Y4) (post booster vaccination administrated in study 10PN-PD-DIT-007)

| **End point values** | Synflorix + Infanrix + Havrix and/or Varilrix Group | Prevenar + Infanrix + Havrix and/or Varilrix Group | Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 253 | 16 | 72 | |
| Units: Titer | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-1 OPA Titers, Y4 (N= 250, 16, 72) | 8.8 (7.1 to 10.9) | 4.6 (3.4 to 6.4) | 8.9 (5.9 to 13.2) | |
| Anti-4 OPA Titers, Y4 (N= 232, 16, 63) | 37.9 (27.2 to 52.8) | 62.2 (13.6 to 284.7) | 50.7 (26.5 to 97) | |
| Anti-5 OPA Titers, Y4 (N= 243, 15, 68) | 7.7 (6.8 to 8.9) | 5.3 (3.5 to 8.1) | 5.5 (4.5 to 6.6) | |
| Anti-6B OPA Titers, Y4 (N= 250, 16, 68) | 875.7 (658.7 to 1164.3) | 978.3 (395.3 to 2421.3) | 716.4 (417.4 to 1229.7) | |
| Anti-7F OPA Titers, Y4 (N= 249, 15, 71) | 1693.1 (1489.3 to 1924.8) | 965.8 (666.8 to 1398.9) | 1602.2 (1286.9 to 1994.5) | |
| Anti-9V OPA Titers, Y4 (N= 250, 15, 70) | 747.4 (624.9 to 894.1) | 563.8 (220.2 to 1444) | 558.6 (403 to 774.2) | |
| Anti-14 OPA Titers, Y4 (N= 250, 15, 71) | 1139.8 (961.9 to 1350.5) | 687.9 (267.8 to 1767.4) | 849.4 (645.4 to 1117.8) | |
| Anti-18C OPA Titers, Y4 (N= 226, 16, 63) | 46.4 (33.3 to 64.5) | 35.3 (8.8 to 142.5) | 26.6 (14.3 to 49.3) | |
| Anti-19F OPA Titers, Y4 (N= 247, 16, 69) | 151.7 (115.9 to 198.4) | 178.8 (64.6 to 495.1) | 129.3 (83.1 to 201.4) | |
| Anti-23F OPA Titers, Y4 (N= 239, 15, 65) | 1518.4 (1107.9 to 2080.9) | 3366.1 (1599.2 to 7085.1) | 1146.2 (596.8 to 2201.3) | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Opsonophagocytic activity (OPA) titers against pneumococcal serotypes [Follow-up Period: Immunogenicity Analysis in Year 4 (111347 sub-study)]

| End point title | Opsonophagocytic activity (OPA) titers against pneumococcal serotypes [Follow-up Period: Immunogenicity Analysis in Year 4 (111347 sub-study)] |
|---|---|

End point description:

Pneumococcal serotypes assessed were OPA-1, OPA-4, OPA-5, OPA-6B, OPA-7F, OPA-9V, OPA-14, OPA-18C, OPA-19F and OPA-23F. The seropositivity cut-off for the assay was ≥ 8. Opsonophagocytic activity was expressed as Geometric Mean Antibody Titers (GMT).

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

End point timeframe:

For primed groups: At Month 48+7 days after additional dose (D7);For unprimed group: at Day 0 (D0) (Pre-vaccination [PRE]), at Day 7 (D7) post dose 1 (of the 2-dose catch-up vaccination) and at Month 3 (M3) post dose 2 (of the 2-dose catch-up vaccination)

| **End point values** | Synflorix + Infanrix + Havrix and/or Varilrix Group | Prevenar + Infanrix + Havrix and/or Varilrix Group | Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix | Unprimed Group |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 204 | 13 | 54 | 96 |
| Units: Titers | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-1 OPA Titers, PRE (N= 0, 0, 0, 94) | 0 (0 to 0) | 0 (0 to 0) | 0 (0 to 0) | 5 (4.2 to 5.9) |
| Anti-1 OPA Titers, D7 (N= 197, 13, 50, 92) | 2920.8 (2353.5 to 3624.7) | 1331 (586.7 to 3019.5) | 1816.1 (1090 to 3025.8) | 605 (462.7 to 791.2) |
| Anti-1 OPA Titers, M3 (N= 0, 0, 0, 95) | 0 (0 to 0) | 0 (0 to 0) | 0 (0 to 0) | 128.3 (97.3 to 169.1) |
| Anti-4 OPA Titers, PRE (N= 0, 0, 0, 81) | 0 (0 to 0) | 0 (0 to 0) | 0 (0 to 0) | 11.5 (7.2 to 18.3) |
| Anti-4 OPA Titers, D7 (N=196, 13, 51, 93) | 23633.7 (19118.5 to 29215.3) | 10650.3 (3969.2 to 28577.6) | 8592.8 (5609.3 to 13163.1) | 18262.1 (15571.6 to 21417.4) |
| Anti-4 OPA Titers, M3 (N= 0, 0, 0, 94) | 0 (0 to 0) | 0 (0 to 0) | 0 (0 to 0) | 4451.3 (3962.4 to 5000.6) |
| Anti-5 OPA Titers, PRE (N= 0, 0, 0, 91) | 0 (0 to 0) | 0 (0 to 0) | 0 (0 to 0) | 4.9 (4.3 to 5.7) |
| Anti-5 OPA Titers, D7 (N= 193, 13, 48, 91) | 822.3 (662.7 to 1020.3) | 375.6 (217.4 to 648.9) | 683.6 (428.6 to 1090.2) | 295.6 (219.4 to 398.3) |
| Anti-5 OPA Titers, M3 (N= 0, 0, 0, 92) | 0 (0 to 0) | 0 (0 to 0) | 0 (0 to 0) | 93.2 (73.7 to 117.8) |

| | | | | |
|---|---|---|---|---|
| Anti-6B OPA Titers, PRE (N= 0, 0, 0, 79) | 0 (0 to 0) | 0 (0 to 0) | 0 (0 to 0) | 70.7 (33.5 to 149.2) |
| Anti-6B OPA Titers, D7 (N= 198, 13, 50, 93) | 3513.1 (2858.1 to 4318.1) | 3566.6 (2446.1 to 5200.3) | 1590.5 (942.8 to 2683.3) | 1971.4 (1238 to 3139.2) |
| Anti-6B OPA Titers, M3 (N= 0, 0, 0, 95) | 0 (0 to 0) | 0 (0 to 0) | 0 (0 to 0) | 2536.9 (2014.1 to 3195.5) |
| Anti-7F OPA Titers, PRE (N= 0, 0, 0, 74) | 0 (0 to 0) | 0 (0 to 0) | 0 (0 to 0) | 1368.2 (849.6 to 2185.8) |
| Anti-7F OPA Titers, D7 (N= 199, 13, 50, 93) | 25196.4 (21149.5 to 30017.6) | 17828.8 (10270.4 to 30949.7) | 13098.6 (9715.5 to 17659.8) | 19243.4 (15701.4 to 23584.5) |
| Anti-7F OPA Titers, M3 (N= 0, 0, 0, 93) | 0 (0 to 0) | 0 (0 to 0) | 0 (0 to 0) | 9692 (8299.3 to 11318.4) |
| Anti-9V OPA Titers, PRE (N= 0, 0, 0, 87) | 0 (0 to 0) | 0 (0 to 0) | 0 (0 to 0) | 398.2 (253.8 to 624.9) |
| Anti-9V OPA Titers, D7 (N=201, 13, 51, 93) | 9419.4 (7586 to 11695.9) | 12234.7 (8280.5 to 18077.3) | 7730.3 (5361.8 to 11145.2) | 8322.7 (6605.7 to 10486.1) |
| Anti-9V OPA Titers, M3 (N= 0, 0, 0, 94) | 0 (0 to 0) | 0 (0 to 0) | 0 (0 to 0) | 6456.1 (5458.1 to 7636.6) |
| Anti-14 OPA Titers, PRE (N= 0, 0, 0, 83) | 0 (0 to 0) | 0 (0 to 0) | 0 (0 to 0) | 586.5 (439 to 783.6) |
| Anti-14 OPA Titers, D7 (N= 197, 13, 51, 94) | 8572.3 (7145.4 to 10284.3) | 4192.8 (2218.6 to 7923.7) | 6883.1 (5057.3 to 9368) | 4678.2 (3788 to 5777.5) |
| Anti-14 OPA Titers, M3 (N= 0, 0, 0, 95) | 0 (0 to 0) | 0 (0 to 0) | 0 (0 to 0) | 4891.1 (4178.8 to 5724.8) |
| Anti-18C OPA Titers, PRE (N= 0, 0, 0, 89) | 0 (0 to 0) | 0 (0 to 0) | 0 (0 to 0) | 5.3 (4.2 to 6.6) |
| Anti-18C OPA Titers, D7 (N= 194, 13, 50, 92) | 3378.9 (2652.2 to 4304.8) | 3478.6 (1788.5 to 6765.8) | 1663.2 (970.5 to 2850.2) | 2503.1 (1692.6 to 3701.6) |
| Anti-18C OPA Titers, M3 (N= 0, 0, 0, 92) | 0 (0 to 0) | 0 (0 to 0) | 0 (0 to 0) | 2255.9 (1876.9 to 2711.4) |
| Anti-19F OPA Titers, PRE (N= 0, 0, 0, 92) | 0 (0 to 0) | 0 (0 to 0) | 0 (0 to 0) | 12 (8.3 to 17.5) |
| Anti-19F OPA Titers, D7 (N= 196, 13, 50, 93) | 1346.4 (1068.6 to 1696.5) | 2340.4 (654.8 to 8365.2) | 662.3 (430 to 1020.1) | 700.2 (456.1 to 1074.9) |
| Anti-19F OPA Titers, M3 (N= 0, 0, 0, 93) | 0 (0 to 0) | 0 (0 to 0) | 0 (0 to 0) | 1437.7 (1146.9 to 1802.3) |
| Anti-23F OPA Titers, PRE (N= 0, 0, 0, 83) | 0 (0 to 0) | 0 (0 to 0) | 0 (0 to 0) | 176.4 (83.4 to 373.2) |
| Anti-23F OPA Titers, D7 (N= 199, 13, 50, 96) | 8700.4 (7021.7 to 10780.5) | 11341.1 (5374.6 to 23931) | 7871.9 (4965.3 to 12480.1) | 6813.9 (5249.5 to 8844.6) |
| Anti-23F OPA Titers, M3 (N= 0, 0, 0, 95) | 0 (0 to 0) | 0 (0 to 0) | 0 (0 to 0) | 5586.1 (4666.1 to 6687.5) |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Antibody concentrations against cross-reactive pneumococcal serotypes 6A and 19A (Anti-6A and - 19A) [Follow-up Period: Persistence Analysis in Year 1 (111345 sub-study)]

| End point title | Antibody concentrations against cross-reactive pneumococcal serotypes 6A and 19A (Anti-6A and - 19A) [Follow-up Period: Persistence Analysis in Year 1 (111345 sub-study)] |
|---|---|

End point description:

The seropositivity cut-off for the assay was ≥ 0.05 µg/mL. Antibody concentrations against 6A and 19A pneumococcal serotypes were determined as Geometric Mean Antibody Concentrations (GMC) and expressed as micrograms per milliliter (µg/mL).

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

End point timeframe:

At Year 1 (Y1) (post booster vaccination administered in study 10PN-PD-DIT-007)

| **End point values** | Synflorix + Infanrix + Havrix and/or Varilrix Group | Prevenar + Infanrix + Havrix and/or Varilrix Group | Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 390 | 31 | 102 | |
| Units: µg/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-6A antibodies, Y1 (N= 390, 31, 102) | 0.28 (0.24 to 0.32) | 0.44 (0.28 to 0.7) | 0.27 (0.21 to 0.36) | |
| Anti-19A antibodies, Y1 (N= 390, 31, 102) | 0.28 (0.25 to 0.32) | 0.21 (0.13 to 0.33) | 0.23 (0.17 to 0.3) | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Antibody concentrations against cross-reactive pneumococcal serotypes 6A and 19A (Anti-6A and - 19A) – Follow-Up Period: Persistence analysis in Year 2 (111346 sub-study)

| End point title | Antibody concentrations against cross-reactive pneumococcal serotypes 6A and 19A (Anti-6A and - 19A) – Follow-Up Period: Persistence analysis in Year 2 (111346 sub-study) |
|---|---|

End point description:

The seropositivity cut-off for the assay was ≥ 0.05 µg/mL. Antibody concentrations against 6A and 19A pneumococcal serotypes were determined as Geometric Mean Antibody Concentrations (GMC) and expressed as micrograms per milliliter (µg/mL).

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

End point timeframe:

At Year 2 (Y2) (post booster vaccination administrated in study 10PN-PDDIT- 007)

| End point values | Synflorix + Infanrix + Havrix and/or Varilrix Group | Prevenar + Infanrix + Havrix and/or Varilrix Group | Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 368 | 30 | 96 | |
| Units: µg/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-6A antibodies, Y2 (N= 368, 30, 96) | 0.33 (0.28 to 0.4) | 0.57 (0.3 to 1.11) | 0.4 (0.27 to 0.58) | |
| Anti-19A antibodies, Y2 (N= 368, 30, 96) | 0.37 (0.31 to 0.44) | 0.25 (0.14 to 0.44) | 0.35 (0.25 to 0.5) | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Antibody concentrations against cross-reactive pneumococcal serotypes 6A and 19A (Anti-6A and - 19A) [Follow-up Period: Persistence Analysis in Year 4 (111347 sub-study)]

| End point title | Antibody concentrations against cross-reactive pneumococcal serotypes 6A and 19A (Anti-6A and - 19A) [Follow-up Period: Persistence Analysis in Year 4 (111347 sub-study)] |
|---|---|

End point description:

Antibody concentrations against 6A and 19A pneumococcal serotypes were determined as Geometric Mean Antibody Concentrations (GMC) and expressed as micro grams per milliliter (µg/mL). The seropositivity cut-off for the assay was ≥ 0.05 µg/mL.

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

End point timeframe:

At Year 4 (Y4) (post booster vaccination administrated in study 10PN-PD-DIT- 007)

| End point values | Synflorix + Infanrix + Havrix and/or Varilrix Group | Prevenar + Infanrix + Havrix and/or Varilrix Group | Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 264 | 19 | 75 | |
| Units: µg/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-6A antibodies, Y4 (N= 263, 19, 74) | 0.92 (0.77 to 1.1) | 0.69 (0.34 to 1.38) | 0.75 (0.55 to 1.03) | |
| Anti-19A antibodies, Y4 (N= 263, 19, 75) | 1.3 (1.07 to 1.59) | 1.08 (0.5 to 2.33) | 1.14 (0.77 to 1.68) | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Antibody concentrations against cross-reactive pneumococcal serotypes 6A and 19A (Anti-6A and 19A) [Follow-up Period: Immunogenicity Analysis in Year 4 (111347 sub-study)]

| End point title | Antibody concentrations against cross-reactive pneumococcal serotypes 6A and 19A (Anti-6A and 19A) [Follow-up Period: Immunogenicity Analysis in Year 4 (111347 sub-study)] |
|---|---|

End point description:

Antibody concentrations against 6A and 19A pneumococcal serotypes were determined as Geometric Mean Antibody Concentrations (GMC) and expressed as micro grams per milliliter (µg/mL). The seropositivity cut-off for the assay was ≥ 0.05 µg/mL.

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

End point timeframe:

For primed groups: At Month 48+7 days after additional dose (D7);For unprimed group: at Day 0 (D0) (Pre-vaccination [PRE]), at Day 7 (D7) post dose 1 (of the 2-dose catch-up vaccination) and at Month 3 (M3) post dose 2 (of the 2-dose catch-up vaccination)

| **End point values** | Synflorix + Infanrix + Havrix and/or Varilrix Group | Prevenar + Infanrix + Havrix and/or Varilrix Group | Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix | Unprimed Group |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 210 | 14 | 55 | 98 |
| Units: µg/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-6A antibodies, PRE (N= 0, 0, 0, 97) | 0 (0 to 0) | 0 (0 to 0) | 0 (0 to 0) | 0.2 (0.15 to 0.27) |
| Anti-6A antibodies, D7 (N= 208, 14, 55, 98) | 2.2 (1.85 to 2.6) | 1.67 (1 to 2.8) | 1.33 (0.96 to 1.83) | 0.44 (0.33 to 0.58) |
| Anti-6A antibodies, M3 (N= 0, 0, 0, 98) | 0 (0 to 0) | 0 (0 to 0) | 0 (0 to 0) | 0.92 (0.73 to 1.16) |
| Anti-19A antibodies, PRE (N= 0, 0, 0, 97) | 0 (0 to 0) | 0 (0 to 0) | 0 (0 to 0) | 0.44 (0.32 to 0.6) |
| Anti-19A antibodies, D7 (N= 208, 14, 54, 98) | 2.79 (2.33 to 3.35) | 2.44 (1.2 to 4.96) | 1.72 (1.14 to 2.61) | 1.1 (0.84 to 1.45) |
| Anti-19A antibodies, M3 (N= 0, 0, 0, 98) | 0 (0 to 0) | 0 (0 to 0) | 0 (0 to 0) | 2.39 (1.9 to 3.01) |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Opsonophagocytic activity (OPA) titers against crossreactive pneumococcal serotypes 6A and 19 A [Follow-up Period: Persistence analysis in Year 1 (111345 sub-study)]

| End point title | Opsonophagocytic activity (OPA) titers against crossreactive pneumococcal serotypes 6A and 19 A [Follow-up Period: Persistence analysis in Year 1 (111345 sub-study)] |
|---|---|

End point description:

Opsonophagocytic activity were assessed for pneumococcal serotypes 6A and 19A (OPA-6A and OPA-19A). The seropositivity cut-off for the assay was ≥ 8. Opsonophagocytic activity was expressed as Geometric Mean Antibody Titers (GMT).

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

End point timeframe:

At Year 1 (Y1) (post booster vaccination administered in study 10PN-PD-DIT-007)

| **End point values** | Synflorix + Infanrix + Havrix and/or Varilrix Group | Prevenar + Infanrix + Havrix and/or Varilrix Group | Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 352 | 26 | 93 | |
| Units: Titers | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-6A OPA Titers, Y1 (N= 323, 25, 75) | 59 (45.9 to 76) | 610.2 (317.7 to 1171.9) | 46.6 (28.3 to 76.8) | |
| Anti-19A OPA Titers, Y1 (N= 155, 26, 93) | 6 (5.2 to 6.8) | 5.9 (3.7 to 9.5) | 5.5 (4.5 to 6.8) | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Opsonophagocytic activity (OPA) titers against crossreactive pneumococcal serotypes 6A and 19 A [Follow-up Period: Persistence analysis in Year 2 (111346 sub-study)]

| End point title | Opsonophagocytic activity (OPA) titers against crossreactive pneumococcal serotypes 6A and 19 A [Follow-up Period: Persistence analysis in Year 2 (111346 sub-study)] |
|---|---|

End point description:

Opsonophagocytic activity were assessed for pneumococcal serotypes 6A and 19A (OPA-6A and OPA-19A). The seropositivity cut-off for the assay was ≥ 8. Opsonophagocytic activity was expressed as Geometric Mean Antibody Titers (GMT).

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

End point timeframe:

At Year 2 (Y2) (post booster vaccination administrated in study 10PN-PD-DIT-007)

| **End point values** | Synflorix + Infanrix + Havrix and/or Varilrix Group | Prevenar + Infanrix + Havrix and/or Varilrix Group | Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 351 | 27 | 91 | |
| Units: Titers | | | | |

| | | | | |
|---|---|---|---|---|
| geometric mean (confidence interval 95%) | | | | |
| Anti-6A OPA Titers, Y2 (N= 314, 25, 82) | 121.8 (95.2 to 156) | 356.5 (134.6 to 944.6) | 133.7 (81.8 to 218.7) | |
| Anti-19A OPA Titers, Y2 (N= 351, 27, 91) | 12.8 (10.4 to 15.7) | 10.9 (5.2 to 22.8) | 11.1 (7.6 to 16.2) | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Opsonophagocytic activity (OPA) titers against crossreactive pneumococcal serotypes 6A and 19 A [Follow-up Period: Persistence Analysis in Year 4 (111347 sub-study)]

| | |
|---|---|
| End point title | Opsonophagocytic activity (OPA) titers against crossreactive pneumococcal serotypes 6A and 19 A [Follow-up Period: Persistence Analysis in Year 4 (111347 sub-study)] |

End point description:

Opsonophagocytic activity were assessed for pneumococcal serotypes 6A and 19A (OPA-6A and OPA-19A). The seropositivity cut-off for the assay was ≥ 8. Opsonophagocytic activity was expressed as Geometric Mean Antibody Titers (GMT).

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

End point timeframe:

At Year 4 (Y4) (post booster vaccination administered in study 10PN-PD-DIT-007)

| End point values | Synflorix + Infanrix + Havrix and/or Varilrix Group | Prevenar + Infanrix + Havrix and/or Varilrix Group | Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 251 | 16 | 71 | |
| Units: Titers | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-6A OPA Titers, Y4 (N= 231, 14, 66) | 213.5 (165.4 to 275.7) | 227.8 (72.1 to 720) | 153.5 (90.5 to 260.2) | |
| Anti-19A OPA Titers, Y4 (N= 246, 15, 68) | 31.2 (23.6 to 41.3) | 14.3 (5.6 to 36.8) | 21.8 (13.3 to 35.7) | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Opsonophagocytic activity (OPA) titers against pneumococcal serotypes 6A and 19A [Follow-up Period: Immunogenicity Analysis in Year 4 (111347 sub-study)]

| | |
|---|---|
| End point title | Opsonophagocytic activity (OPA) titers against pneumococcal serotypes 6A and 19A [Follow-up Period: Immunogenicity |

| | |
|---|---|
| | Analysis in Year 4 (111347 sub-study)] |

End point description:

Opsonophagocytic activity were assessed for pneumococcal serotypes 6A and 19A (OPA-6A and OPA-19A). The seropositivity cut-off for the assay was ≥ 8. Opsonophagocytic activity was expressed as Geometric Mean Antibody Titers (GMT).

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

End point timeframe:

For primed groups: At Month 48+7 days after additional dose (D7);For unprimed group: at Day 0 (D0) (Pre-vaccination [PRE]), at Day 7 (D7) post dose 1 (of the 2-dose catch-up vaccination) and at Month 3 (M3) post dose 2 (of the 2-dose catch-up vaccination)

| **End point values** | Synflorix + Infanrix + Havrix and/or Varilrix Group | Prevenar + Infanrix + Havrix and/or Varilrix Group | Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix | Unprimed Group |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 201 | 13 | 50 | 92 |
| Units: Titers | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-6A OPA Titers, PRE (N= 0, 0, 0, 82) | 0 (0 to 0) | 0 (0 to 0) | 0 (0 to 0) | 102.6 (61.5 to 171.2) |
| Anti-6A OPA Titers, D7 (N= 189, 12, 49, 90) | 1217.7 (957.8 to 1548.2) | 1490.2 (681.6 to 3257.8) | 467.7 (293.8 to 744.5) | 826.5 (593.9 to 1150.2) |
| Anti-6A OPA Titers, M3 (N= 0, 0, 0, 91) | 0 (0 to 0) | 0 (0 to 0) | 0 (0 to 0) | 943.4 (691.3 to 1287.4) |
| Anti-19A OPA Titers, PRE (N= 0, 0, 0, 92) | 0 (0 to 0) | 0 (0 to 0) | 0 (0 to 0) | 9.9 (7 to 13.8) |
| Anti-19A OPA Titers, D7 (N= 194, 13, 48, 90) | 467 (335 to 651.1) | 437.6 (81.3 to 2356.3) | 106.1 (54.1 to 208.3) | 431.2 (269.4 to 689.9) |
| Anti-19A OPA Titers, M3 (N= 0, 0, 0, 91) | 0 (0 to 0) | 0 (0 to 0) | 0 (0 to 0) | 376.4 (256.3 to 552.6) |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Antibody concentrations to protein D (Anti-PD) - Follow-up Period: Persistence analysis in Year 1 (111345 sub-study)

| | |
|---|---|
| End point title | Antibody concentrations to protein D (Anti-PD) - Follow-up Period: Persistence analysis in Year 1 (111345 sub-study) |

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.

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

End point timeframe:

At Year 1 (Y1) (post booster vaccination administered in study 10PN-PD-DIT-007)

| End point values | Synflorix + Infanrix + Havrix and/or Varilrix Group | Prevenar + Infanrix + Havrix and/or Varilrix Group | Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 390 | 30 | 102 | |
| Units: EL.U/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-PD antibodies, Y1 (N= 390, 30, 102) | 822.1 (731.5 to 923.9) | 93.9 (66.6 to 132.3) | 193.6 (155.9 to 240.4) | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Antibody concentrations to protein D (Anti-PD) – Follow-up Period: Persistence analysis in Year 2 (111346 sub-study)

| End point title | Antibody concentrations to protein D (Anti-PD) – Follow-up Period: Persistence analysis in Year 2 (111346 sub-study) |
|---|---|

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.

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

End point timeframe:

At Year 2 (Y2) (post booster vaccination administered in study 10PN-PD-DIT- 007)

| End point values | Synflorix + Infanrix + Havrix and/or Varilrix Group | Prevenar + Infanrix + Havrix and/or Varilrix Group | Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 368 | 29 | 96 | |
| Units: EL.U/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-PD antibodies, Y2 (N= 368, 29, 96) | 573.2 (509.6 to 644.8) | 116.7 (80.9 to 168.3) | 157.5 (128.7 to 192.8) | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Antibody concentrations to protein D (Anti-PD) [Follow-up Period: Persistence Analysis in Year 4 (111347 sub-study)]

| End point title | Antibody concentrations to protein D (Anti-PD) [Follow-up Period: Persistence Analysis in Year 4 (111347 sub-study)] |
|---|---|

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.

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

End point timeframe:

At Year 4 (Y4) (post booster vaccination administered in study 10PN-PD-DIT- 007)

| End point values | Synflorix + Infanrix + Havrix and/or Varilrix Group | Prevenar + Infanrix + Havrix and/or Varilrix Group | Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 264 | 19 | 75 | |
| Units: EL.U/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-PD antibodies, Y4 (N= 261, 19, 74) | 372.4 (329.6 to 420.9) | 144.9 (86.3 to 243.2) | 161.4 (128.4 to 203) | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Antibody concentrations to protein D (Anti-PD) [Follow-up Period: Immunogenicity Analysis in Year 4 (111347 sub-study)]

| End point title | Antibody concentrations to protein D (Anti-PD) [Follow-up Period: Immunogenicity Analysis in Year 4 (111347 sub-study)] |
|---|---|

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.

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

End point timeframe:

For primed groups: At Month 48+7 days after additional dose (D7);For unprimed group: at Day 0 (D0) (Pre-vaccination [PRE]), at Day 7 (D7) post dose 1 (of the 2-dose catch-up vaccination) and at Month 3 (M3) post dose 2 (of the 2-dose catch-up vaccination)

| End point values | Synflorix + Infanrix + Havrix and/or Varilrix Group | Prevenar + Infanrix + Havrix and/or Varilrix Group | Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix | Unprimed Group |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 208 | 14 | 54 | 98 |
| Units: EL.U/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-PD antibodies, PRE (N= 0, 0, 0, 95) | 0 (0 to 0) | 0 (0 to 0) | 0 (0 to 0) | 106 (91.1 to 123.4) |
| Anti-PD antibodies, D7 (N= 208, 14, 54, 98) | 2106 (1806.7 to 2454.9) | 718.2 (442.5 to 1165.7) | 680.7 (522.9 to 886.2) | 382.9 (320.7 to 457.2) |
| Anti-PD antibodies, M3 (N= 0, 0, 0, 98) | 0 (0 to 0) | 0 (0 to 0) | 0 (0 to 0) | 708.6 (604.6 to 830.4) |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects reported with solicited local symptoms

| End point title | Number of subjects reported with solicited local symptoms |
|---|---|

End point description:

Solicited local symptoms assessed were pain, redness and swelling. Any occurrence of symptom regardless of intensity grade. Any Redness or any Swelling symptom = any symptom greater than (>) 0 millimeter (mm). Grade 3 pain = maximum intensity of local injection defined as subject crying when limb was moved/spontaneously painful. Grade 3 redness/swelling= maximum intensity of local injection >30 mm. Follow-up period was of 4 days (Days 0-3) after Synflorix vaccination in Year 4 Persistence and Immunological Memory 111347 Study, thus one period of 4 days for primed subjects and 2 periods of 4 days for unprimed subjects.

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

End point timeframe:

Within 4 days (Days 0-3) period(s) after Synflorix vaccination in Year 4 Persistence and Immunological Memory 111347 Study

| End point values | Synflorix + Infanrix + Havrix and/or Varilrix Group | Prevenar + Infanrix + Havrix and/or Varilrix Group | Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix | Unprimed Group |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 264 | 20 | 64 | 100 |
| Units: Participants | | | | |
| Pain, Any (N= 264, 20, 64, 100) | 157 | 9 | 34 | 54 |
| Redness, Any (N= 264, 20, 64, 100) | 90 | 5 | 14 | 21 |
| Swelling, Any (N= 264, 20, 64, 100) | 67 | 4 | 15 | 20 |
| Pain, Grade 3 (N= 264, 20, 64, 100) | 7 | 1 | 5 | 3 |
| Redness, Grade 3 (> 30 mm) (N= 264, 20, 64, 100) | 7 | 0 | 0 | 1 |
| Swelling, Grade 3 (> 30 mm) (N= 264, 20, 64, 100) | 5 | 0 | 1 | 2 |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects reported with solicited general symptoms

| End point title | Number of subjects reported with solicited general symptoms |
|---|---|

End point description:

Solicited general symptoms assessed were drowsiness, irritability, loss of appetite and fever (any fever defined as temperature by axillary measurement of 37.5°C and above). Grade 3 drowsiness was defined as drowsiness that prevented normal activity; Grade 3 irritability was defined as crying that could not be comforted/prevented normal activity. Grade 3 loss of appetite was defined as subject not eating at all. Grade 3 fever was defined as axillary temperature >39.5°C. Related AE was defined as any AE assessed by investigators to be causally related to administration of the study vaccine. Follow-up period was of 4 days (Days 0-3) after Synflorix vaccination in Year 4 Persistence and Immunological Memory 111347 Study, thus one period of 4 days for primed subjects and 2 periods of 4 days for unprimed subjects.

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

End point timeframe:

Within 4 days (Days 0-3) period(s) after Synflorix vaccination in Year 4 Persistence and Immunological Memory 111347 Study

| **End point values** | Synflorix + Infanrix + Havrix and/or Varilrix Group | Prevenar + Infanrix + Havrix and/or Varilrix Group | Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix | Unprimed Group |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 263 | 20 | 64 | 100 |
| Units: Participants | | | | |
| Drowsiness, Any (N= 263, 20, 64, 100) | 49 | 2 | 12 | 12 |
| Drowsiness, Grade 3 (N= 263, 20, 64, 100) | 1 | 0 | 0 | 0 |
| Drowsiness, Related (N= 263, 20, 64, 100) | 48 | 2 | 11 | 11 |
| Irritability, Any (N= 263, 20, 64, 100) | 35 | 4 | 6 | 8 |
| Irritability, Related (N= 263, 20, 64, 100) | 35 | 4 | 6 | 8 |
| Irritability, Grade 3 (N= 263, 20, 64, 100) | 0 | 0 | 0 | 0 |
| Loss of appetite, Any (N= 263, 20, 64, 100) | 30 | 3 | 6 | 13 |
| Loss of appetite, Grade 3 (N= 263, 20, 64, 100) | 1 | 0 | 1 | 0 |
| Loss of appetite, Related (N= 263, 20, 64, 100) | 30 | 3 | 5 | 11 |
| Fever, Any (N= 263, 20, 64, 100) | 13 | 0 | 2 | 5 |
| Fever, >39,5°C (N= 263, 20, 64, 100) | 0 | 0 | 0 | 0 |
| Fever, Related (N= 263, 20, 64, 100) | 13 | 0 | 1 | 5 |

## Statistical analyses

No statistical analyses for this end point

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

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

End point description:

An AE is any untoward medical occurrence in a clinical investigation subject, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. "Any" was defined an incidence of an unsolicited AE regardless of intensity or relationship to study vaccination. Follow-up period was of 31 days (Days 0-30) after Synflorix vaccination in Year 4 Persistence and Immunological Memory 111347 Study, thus one period of 31 days for primed subjects and 2 periods of 31 days for unprimed subjects.

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

End point timeframe:

Within 31 days (Day 0-30) after Synflorix vaccination in Year 4 Persistence and Immunological Memory 111347 Study

| **End point values** | Synflorix + Infanrix + Havrix and/or Varilrix Group | Prevenar + Infanrix + Havrix and/or Varilrix Group | Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix | Unprimed Group |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 264 | 20 | 65 | 100 |
| Units: Participants | | | | |
| Any Unsolicited AEs (N= 264, 20, 65, 100) | 25 | 0 | 3 | 6 |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with serious adverse events (SAEs) related to study procedures [Follow-up Period: Year 1 (111345 sub-study)]

| End point title | Number of subjects with serious adverse events (SAEs) related to study procedures [Follow-up Period: Year 1 (111345 sub-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" was defined an incidence of a SAE regardless of intensity/severity.

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

End point timeframe:

During Year 1 (Y1) (post booster vaccination administered in study 10PN-PD-DIT-007) i.e. for each primed subject: from the time the subject was enrolled in the 111345 study until he/she completed the same study (approximatively 12 months)

| **End point values** | Synflorix + Infanrix + Havrix and/or Varilrix Group | Prevenar + Infanrix + Havrix and/or Varilrix Group | Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 391 | 31 | 102 | |
| Units: Participants | | | | |
| Any Related SAEs, Y1 (N=391, 31, 102) | 1 | 0 | 0 | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with serious adverse events (SAEs) related to study procedures [(Follow-up Period: Year 2 (111346 sub-study) until Year 4 (111347 sub-study)]

| End point title | Number of subjects with serious adverse events (SAEs) related to study procedures [(Follow-up Period: Year 2 (111346 sub-study) until Year 4 (111347 sub-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 an incidence of a SAE regardless of intensity/severity.

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

End point timeframe:

From Year (Y) 2 to Y4 FU visit (post booster vaccination administered in 10PN-PD-DIT-007) i.e. for each subject(S): when S was enrolled in 111346 study until S completed the same study visit or the 111347 study visit (range of 1 to 3 years for each S))

| **End point values** | Synflorix + Infanrix + Havrix and/or Varilrix Group | Prevenar + Infanrix + Havrix and/or Varilrix Group | Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 370 | 31 | 96 | |
| Units: Participants | | | | |
| Any Related SAEs, Y2 to Y4, (N= 370, 31, 96) | 0 | 0 | 0 | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with serious adverse events (SAEs) [Follow-up Period: Vaccination Period in Year 4 (111347 sub-study)]

| End point title | Number of subjects with serious adverse events (SAEs) [Follow-up Period: Vaccination Period in Year 4 (111347 sub-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 an incidence of a SAE regardless of intensity/severity.

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

End point timeframe:

For primed groups: from Months 48-49 (additional vaccination period); for unprimed group: from Day 0 up to Month 3 (catch-up vaccination period)

| End point values | Synflorix + Infanrix + Havrix and/or Varilrix Group | Prevenar + Infanrix + Havrix and/or Varilrix Group | Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix | Unprimed Group |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 264 | 20 | 65 | 100 |
| Units: Participants | | | | |
| Any Related SAEs, Y4 (N= 264, 20, 65, 100) | 0 | 0 | 0 | 0 |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of seropositive subjects for opsonophagocytic activity against pneumococcal serotypes [Follow-up Period: Persistence analysis in Year 1 (111345 sub-study)]

| End point title | Number of seropositive subjects for opsonophagocytic activity against pneumococcal serotypes [Follow-up Period: Persistence analysis in Year 1 (111345 sub-study)] |
|---|---|

End point description:

A seropositive subject was a subject whose antibody concentration was greater than or equal to (≥) the cut-off value. Pneumococcal serotypes assessed were 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F. The seropositivity cut-off for the assay was 8.

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

End point timeframe:

At Year 1 (Y1) (post booster vaccination administered in study 10PN-PD-DIT-007)

| End point values | Synflorix + Infanrix + Havrix and/or Varilrix Group | Prevenar + Infanrix + Havrix and/or Varilrix Group | Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 359 | 27 | 94 | |
| Units: Participants | | | | |
| Anti-1 OPA, Y1 (N= 354, 27, 92) | 188 | 2 | 26 | |
| Anti-4 OPA, Y1 ( N= 340, 26, 86) | 201 | 21 | 65 | |
| Anti-5 OPA, Y1 (N= 335, 27, 89 | 241 | 2 | 46 | |
| Anti-6B OPA, Y1 (N= 354, 25, 88) | 164 | 23 | 44 | |
| Anti-7F OPA, Y1 (N= 346, 25, 89) | 343 | 20 | 85 | |
| Anti-9V OPA, Y1 (N= 352, 26, 94) | 351 | 26 | 90 | |
| Anti-14 OPA, Y1 (N= 343, 25, 91) | 336 | 25 | 89 | |
| Anti-18C OPA, Y1 (N= 319, 24, 84) | 173 | 10 | 25 | |
| Anti-19F OPA, Y1 (N= 359, 27, 93) | 306 | 19 | 83 | |
| Anti-23F OPA, Y1 (N=336, 27, 93) | 301 | 26 | 82 | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of seropositive subjects for opsonophagocytic activity against pneumococcal serotypes [Follow-up Period: persistence analysis in Year 2 (111346 sub-study)]

| End point title | Number of seropositive subjects for opsonophagocytic activity against pneumococcal serotypes [Follow-up Period: persistence analysis in Year 2 (111346 sub-study)] |
|---|---|

End point description:

A seropositive subject was a subject whose antibody concentration was greater than or equal to (≥) the cut-off value. Pneumococcal serotypes assessed were 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F. The seropositivity cut-off for the assay was 8.

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

End point timeframe:

At Year 2 (Y2) (post booster vaccination administered in study 10PN-PD-DIT-007)

| End point values | Synflorix + Infanrix + Havrix and/or Varilrix Group | Prevenar + Infanrix + Havrix and/or Varilrix Group | Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 354 | 27 | 92 | |
| Units: Participants | | | | |
| Anti-1 OPA, Y2 (N= 354, 27, 92) | 92 | 0 | 15 | |
| Anti-4 OPA, Y2 (N= 335, 27, 84) | 146 | 12 | 48 | |
| Anti-5 OPA, Y2 (N= 351, 27, 91) | 169 | 2 | 31 | |
| Anti-6B OPA, Y2 (N= 342, 27, 88) | 241 | 24 | 67 | |
| Anti-7F OPA Titers, Y2 (N= 350, 27, 91) | 350 | 26 | 90 | |

| | | | | |
|---|---|---|---|---|
| Anti-9V OPA, Y2 (N= 349, 27, 92) | 247 | 27 | 87 | |
| Anti-14 OPA, Y2 (N= 341, 25, 90) | 333 | 24 | 85 | |
| Anti-18C OPA, Y2 (N= 325, 27, 83) | 165 | 11 | 29 | |
| Anti-19F OPA, Y2 (N= 349, 27, 92) | 279 | 21 | 78 | |
| Anti-23F OPA, Y2 (N= 342, 26, 91) | 285 | 25 | 72 | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of seropositive subjects for opsonophagocytic activity against pneumococcal serotypes [Follow-up Period: Persistence Analysis in Year 4 (111347 sub-study)]

| End point title | Number of seropositive subjects for opsonophagocytic activity against pneumococcal serotypes [Follow-up Period: Persistence Analysis in Year 4 (111347 sub-study)] |
|---|---|

End point description:

A seropositive subject was a subject whose antibody concentration was greater than or equal to (≥) the cut-off value. Pneumococcal serotypes assessed were 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F. The seropositivity cut-off for the assay was 8.

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

End point timeframe:

At Year 4 (Y4) (post booster vaccination administered in study 10PN-PD-DIT-007)

| End point values | Synflorix + Infanrix + Havrix and/or Varilrix Group | Prevenar + Infanrix + Havrix and/or Varilrix Group | Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 250 | 16 | 72 | |
| Units: Participants | | | | |
| Anti-1 OPA, Y4 (N= 250, 16, 72) | 55 | 1 | 17 | |
| Anti-4 OPA, Y4 (N= 232, 16, 63) | 107 | 8 | 33 | |
| Anti-5 OPA, Y4 (N= 243, 15, 68) | 80 | 2 | 11 | |
| Anti-6B OPA, Y4 (N= 250, 16, 68) | 223 | 15 | 62 | |
| Anti-7F OPA, Y4 (N= 249, 15, 71) | 248 | 15 | 71 | |
| Anti-9V OPA, Y4 (N= 250, 15, 70) | 242 | 14 | 68 | |
| Anti-14 OPA, Y4 (N= 250, 15, 71) | 247 | 14 | 70 | |
| Anti-18C OPA, Y4 (N= 226, 16, 63) | 121 | 8 | 27 | |
| Anti-19F OPA, Y4 (N= 247, 16, 69) | 211 | 14 | 62 | |
| Anti-23F OPA, Y4 (N= 239, 15, 65) | 209 | 15 | 55 | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of seropositive subjects for opsophagocytic activity against pneumococcal serotypes [Follow-up Period: Immunogenicity Analysis in Year 4 (111347 sub-study)]

| End point title | Number of seropositive subjects for opsophagocytic activity against pneumococcal serotypes [Follow-up Period: Immunogenicity Analysis in Year 4 (111347 sub-study)] |
|---|---|

End point description:

A seropositive subject was a subject whose antibody concentration was greater than or equal to (≥) the cut-off value. Pneumococcal serotypes assessed were 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F. Analysis was performed with Unprimed group included. The seropositivity cut-off for the assay was 8.

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

End point timeframe:

For primed groups: At Month 48+7 days after additional dose (D7);For unprimed group: at Day 0 (D0) (Pre-vaccination [PRE]), at Day 7 (D7) post dose 1 (of the 2-dose catch-up vaccination) and at Month 3 (M3) post dose 2 (of the 2-dose catch-up vaccination)

| End point values | Synflorix + Infanrix + Havrix and/or Varilrix Group | Prevenar + Infanrix + Havrix and/or Varilrix Group | Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix | Unprimed Group |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 201 | 13 | 51 | 96 |
| Units: Participants | | | | |
| Anti-1 OPA, PRE (N= 0, 0, 0, 94) | 0 | 0 | 0 | 8 |
| Anti-1 OPA, D7 (N= 197, 13, 50, 92) | 193 | 13 | 48 | 90 |
| Anti-1 OPA, M3 (N= 0, 0, 0, 95) | 0 | 0 | 0 | 87 |
| Anti-4 OPA, PRE (N= 0, 0, 0, 81) | 0 | 0 | 0 | 17 |
| Anti-4 OPA, D7 (N= 196, 13, 51, 93) | 194 | 13 | 50 | 93 |
| Anti-4 OPA, M3 (N= 0, 0, 0, 94) | 0 | 0 | 0 | 94 |
| Anti-5 OPA, PRE (N= 0, 0, 0, 92) | 0 | 0 | 0 | 8 |
| Anti-5 OPA, D7 (N= 193, 13, 48, 91) | 186 | 13 | 47 | 87 |
| Anti-5 OPA, M3 (N= 0, 0, 0, 92) | 0 | 0 | 0 | 89 |
| Anti-6B OPA, PRE (N= 0, 0, 0, 79) | 0 | 0 | 0 | 35 |
| Anti-6B OPA, D7 (N= 198, 13, 50, 93) | 196 | 13 | 48 | 84 |
| Anti-6B OPA, M3 (N= 0, 0, 0, 95) | 0 | 0 | 0 | 94 |
| Anti-7F OPA, PRE (N= 0, 0, 0, 74) | 0 | 0 | 0 | 67 |
| Anti-7F OPA, D7 (N= 199, 13, 50, 93) | 199 | 13 | 50 | 93 |
| Anti-7F OPA, M3 (N= 0, 0, 0, 93) | 0 | 0 | 0 | 93 |
| Anti-9V OPA, PRE (N= 0, 0, 0, 87) | 0 | 0 | 0 | 87 |
| Anti-9V OPA, D7 (N= 201, 13, 51, 93) | 201 | 13 | 51 | 93 |
| Anti-9V OPA, M3 (N= 0, 0, 0, 94) | 0 | 0 | 0 | 94 |
| Anti-14 OPA, PRE (N= 0, 0, 0, 83) | 0 | 0 | 0 | 81 |
| Anti-14 OPA, D7 (N= 197, 13, 51, 94) | 197 | 13 | 51 | 94 |
| Anti-14 OPA, M3 (N= 0, 0, 0, 95) | 0 | 0 | 0 | 95 |
| Anti-18C OPA, PRE (N= 0, 0, 0, 89) | 0 | 0 | 0 | 7 |
| Anti-18C OPA, D7 (N= 194, 13, 50, 92) | 190 | 13 | 48 | 88 |
| Anti-18C OPA, M3 (N= 0, 0, 0, 92) | 0 | 0 | 0 | 92 |
| Anti-19F OPA, PRE (N= 0, 0, 0, 92) | 0 | 0 | 0 | 30 |
| Anti-19F OPA, D7 (N= 196, 13, 50, 93) | 194 | 13 | 50 | 91 |
| Anti-19F OPA, M3 (N= 0, 0, 0, 93) | 0 | 0 | 0 | 93 |
| Anti-23F OPA, PRE (N= 0, 0, 0, 83) | 0 | 0 | 0 | 47 |

| | | | | |
|---|---|---|---|---|
| Anti-23F OPA, D7 (N= 199, 13, 50, 96) | 197 | 13 | 49 | 95 |
| Anti-23F OPA, M3 (N= 0, 0, 0, 95) | 0 | 0 | 0 | 95 |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of seropositive subjects for anti-pneumococcal cross-reactive serotypes 6A and 19A [Follow-up Period: persistence analysis in Year 1 (111345 sub-study)]

| End point title | Number of seropositive subjects for anti-pneumococcal cross-reactive serotypes 6A and 19A [Follow-up Period: persistence analysis in Year 1 (111345 sub-study)] |
|---|---|

End point description:

A seropositive subject was a subject whose antibody concentration was greater than or equal to (≥) the cut-off value. Pneumococcal serotypes assessed were 6A and 19A. The results for the immune responses were measured by 22F-inhibition ELISA. The seropositivity cut-off for the assay was 0.05 µg/mL.

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

End point timeframe:

At Year 1 (Y1) (post booster vaccination administered in study 10PN-PD-DIT-007)

| End point values | Synflorix + Infanrix + Havrix and/or Varilrix Group | Prevenar + Infanrix + Havrix and/or Varilrix Group | Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 390 | 31 | 102 | |
| Units: Participants | | | | |
| Anti-6A antibodies, Y1 (N= 390, 31, 102) | 376 | 31 | 97 | |
| Anti-19A antibodies, Y1 (N= 390, 31, 102) | 366 | 29 | 93 | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of seropositive subjects for anti-pneumococcal cross-reactive serotypes 6A and 19A [Follow-up Period: Persistence analysis in Year 2 (111346 sub-study)]

| End point title | Number of seropositive subjects for anti-pneumococcal cross-reactive serotypes 6A and 19A [Follow-up Period: Persistence analysis in Year 2 (111346 sub-study)] |
|---|---|

End point description:

A seropositive subject was a subject whose antibody concentration was greater than or equal to (≥) the cut-off value. Pneumococcal serotypes assessed were 6A and 19A. The immune responses were

measured by 22F-inhibation ELISA. The seropositivity cut-off for the assay was 0.05 µg/mL.

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

End point timeframe:

At Year 2 (Y2) (post booster vaccination administered in study 10PN-PD-DIT-007)

| **End point values** | Synflorix + Infanrix + Havrix and/or Varilrix Group | Prevenar + Infanrix + Havrix and/or Varilrix Group | Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 368 | 30 | 96 | |
| Units: Participants | | | | |
| Anti-6A antibodies, Y2 (N= 368, 30, 96) | 330 | 30 | 86 | |
| Anti-19A antibodies, Y2 (N= 368, 30, 96) | 319 | 25 | 83 | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of seropositive subjects for anti-pneumococcal cross-reactive serotypes 6A and 19A [Follow-up Period: Persistence Analysis in Year 4 (111347 sub-study)]

| End point title | Number of seropositive subjects for anti-pneumococcal cross-reactive serotypes 6A and 19A [Follow-up Period: Persistence Analysis in Year 4 (111347 sub-study)] |
|---|---|

End point description:

A seropositive subject was a subject whose antibody concentration was greater than or equal to (≥) the cut-off value. Pneumococcal serotypes assessed were 6A and 19A. The immune responses were measured by 22F-inhibition ELISA. The seropositivity cut-off for the assay was 0.05 µg/mL.

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

End point timeframe:

At Year 4 (Y4) (post booster vaccination administered in study 10PN-PD-DIT-007)

| **End point values** | Synflorix + Infanrix + Havrix and/or Varilrix Group | Prevenar + Infanrix + Havrix and/or Varilrix Group | Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 263 | 19 | 75 | |
| Units: Participants | | | | |
| Anti-6A antibodies, Y4 (N= 263, 31, 75) | 256 | 18 | 72 | |
| Anti-19A antibodies, Y4 (N= 263, 31, 75) | 260 | 18 | 74 | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of seropositive subjects for anti-pneumococcal cross-reactive serotypes 6A and 19A [Follow-up Period: Immunogenicity Analysis in Year 4 (111347 sub-study)]

| End point title | Number of seropositive subjects for anti-pneumococcal cross-reactive serotypes 6A and 19A [Follow-up Period: Immunogenicity Analysis in Year 4 (111347 sub-study)] |
|---|---|

End point description:

A seropositive subject was a subject whose antibody concentration was greater than or equal to (≥) the cut-off value. Pneumococcal serotypes assessed were 6A and 19A. The immune responses were measured by 22F-inhibition ELISA. The seropositivity cut-off for the assay was 0.05 µg/mL.

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

End point timeframe:

For primed groups: At Month 48+7 days after additional dose (D7);For unprimed group: at Day 0 (D0) (Pre-vaccination [PRE]), at Day 7 (D7) post dose 1 (of the 2-dose catch-up vaccination) and at Month 3 (M3) post dose 2 (of the 2-dose catch-up vaccination)

| End point values | Synflorix + Infanrix + Havrix and/or Varilrix Group | Prevenar + Infanrix + Havrix and/or Varilrix Group | Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix | Unprimed Group |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 208 | 14 | 54 | 98 |
| Units: Participants | | | | |
| Anti-6A antibodies, PRE (N= 0, 0, 0, 97) | 0 | 0 | 0 | 76 |
| Anti-6A antibodies, D7 (N= 208, 14, 54, 98) | 208 | 14 | 54 | 92 |
| Anti-6A antibodies, M3 (N= 0, 0, 0, 98) | 0 | 0 | 0 | 97 |
| Anti-19A antibodies, PRE (N= 0, 0, 0, 97) | 0 | 0 | 0 | 88 |
| Anti-19A antibodies, D7 (N= 208, 14, 54, 98) | 208 | 14 | 54 | 97 |
| Anti-19A antibodies, M3 (N= 0, 0, 0, 98) | 0 | 0 | 0 | 98 |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of seropositive subjects for opsonophagocytic activity against

**pneumococcal cross-reactive serotypes 6A and 19A [Follow-up Period: Persistence analysis in Year 1 (111345 sub-study)]**

| End point title | Number of seropositive subjects for opsonophagocytic activity against pneumococcal cross-reactive serotypes 6A and 19A [Follow-up Period: Persistence analysis in Year 1 (111345 sub-study)] |
|---|---|

End point description:

A seropositive subject was a subject whose antibody concentration was greater than or equal to (≥) the cut-off value. Pneumococcal serotypes assessed were 6A and 19A. The immune responses were mesured by Opsonophagocytic activity (OPA). The seropositivity cut-off for the assay was 8.

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

End point timeframe:

At Year 1 (Y1) (post booster vaccination administered in study 10PN-PD-DIT-007)

| **End point values** | Synflorix + Infanrix + Havrix and/or Varilrix Group | Prevenar + Infanrix + Havrix and/or Varilrix Group | Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 352 | 26 | 93 | |
| Units: Participants | | | | |
| Anti-6A OPA, Y1 (N= 323, 25, 75) | 196 | 24 | 45 | |
| Anti-19A OPA, Y1 (352, 26, 93) | 45 | 3 | 10 | |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Number of seropositive subjects for opsonophagocytic activity against pneumococcal cross-reactive serotypes 6A and 19A [Follow-up Period: Persistence Analysis in Year 2 (111346 sub-study)]**

| End point title | Number of seropositive subjects for opsonophagocytic activity against pneumococcal cross-reactive serotypes 6A and 19A [Follow-up Period: Persistence Analysis in Year 2 (111346 sub-study)] |
|---|---|

End point description:

A seropositive subject was a subject whose antibody concentration was greater than or equal to (≥) the cut-off value. Pneumococcal serotypes assessed were 6A and 19A. The immune responses were measured by Opsonophagocytic activity (OPA). The seropositivity cut-off for the assay was 8.

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

End point timeframe:

At Year 2 (Y2) (post booster vaccination administered in study 10PN-PD-DIT-007)

| End point values | Synflorix + Infanrix + Havrix and/or Varilrix Group | Prevenar + Infanrix + Havrix and/or Varilrix Group | Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 351 | 27 | 91 | |
| Units: Participants | | | | |
| Anti-6A OPA, Y2 (N= 314, 25, 82) | 235 | 21 | 62 | |
| Anti-19A OPA, Y2 (N= 351, 27, 91) | 115 | 8 | 29 | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of seropositive subjects for opsonophagocytic activity against pneumococcal cross-reactive serotypes 6A and 19A [Follow-up Period: Persistence Analysis in Year 4 (111347 sub-study)]

| End point title | Number of seropositive subjects for opsonophagocytic activity against pneumococcal cross-reactive serotypes 6A and 19A [Follow-up Period: Persistence Analysis in Year 4 (111347 sub-study)] |
|---|---|

End point description:

A seropositive subject was a subject whose antibody concentration was greater than or equal to (≥) the cut-off value. Pneumococcal serotypes assessed were 6A and 19A. The immune responses were measured by Opsonophagocytic Activity (OPA). The seropositivity cut-off for the assay was 8.

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

End point timeframe:

At Year 4 (Y4) (post booster vaccination administered in study 10PN-PD-DIT-007)

| End point values | Synflorix + Infanrix + Havrix and/or Varilrix Group | Prevenar + Infanrix + Havrix and/or Varilrix Group | Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 246 | 15 | 68 | |
| Units: Participants | | | | |
| Anti-6A OPA Titers, Y4 (N= 231, 14, 66) | 194 | 12 | 51 | |
| Anti-19A OPA Titers, Y4 (N= 246, 15, 68) | 135 | 7 | 34 | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of seropositive subjects for opsonophagocytic activity against pneumococcal cross-reactive serotypes 6A and 19A [Follow-up Period: Immunogenicity Analysis in Year 4 (111347 sub-study)]

| End point title | Number of seropositive subjects for opsonophagocytic activity against pneumococcal cross-reactive serotypes 6A and 19A [Follow-up Period: Immunogenicity Analysis in Year 4 (111347 sub-study)] |
|---|---|

End point description:

A seropositive subject was a subject whose antibody concentration was greater than or equal to (≥) the cut-off value. Pneumococcal serotypes assessed were 6A and 19A. The immune responses were measured by Opsonophagocytic Activity (OPA). The seropositivity cut-off for the assay was 8.

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

End point timeframe:

For primed groups: At Month 48+7 days after additional dose (D7);For unprimed group: at Day 0 (D0) (Pre-vaccination [PRE]), at Day 7 (D7) post dose 1 (of the 2-dose catch-up vaccination) and at Month 3 (M3) post dose 2 (of the 2-dose catch-up vaccination)

| **End point values** | Synflorix + Infanrix + Havrix and/or Varilrix Group | Prevenar + Infanrix + Havrix and/or Varilrix Group | Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix | Unprimed Group |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 194 | 13 | 49 | 92 |
| Units: Participants | | | | |
| Anti-6A OPA, PRE (N= 0, 0, 0, 82) | 0 | 0 | 0 | 57 |
| Anti-6A OPA, D7 (N= 189, 12, 49, 92) | 185 | 12 | 46 | 88 |
| Anti-6A OPA, M3 (N= 0, 0, 0, 91) | 0 | 0 | 0 | 87 |
| Anti-19A OPA, PRE (N= 0, 0, 0, 92) | 0 | 0 | 0 | 25 |
| Anti-19A OPA, D7 (N= 194, 13, 48, 90) | 173 | 11 | 36 | 81 |
| Anti-19A OPA, M3 (N= 0, 0, 0, 91) | 0 | 0 | 0 | 87 |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of seropositive subjects for anti-protein D (Anti-PD) [Follow-up Period: Persistence analysis in Year 1 (111345 sub-study)]

| End point title | Number of seropositive subjects for anti-protein D (Anti-PD) [Follow-up Period: Persistence analysis in Year 1 (111345 sub-study)] |
|---|---|

End point description:

A seropositive subject was a subject whose anti-PD antibody concentration was greater than or equal to (≥) the cut-off value. The seropositivity cut-off for the assay was 100 EL.U/ML.

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

End point timeframe:

At Year 1 (Y1) (post booster vaccination administered in study 10PN-PD-DIT-007)

| End point values | Synflorix + Infanrix + Havrix and/or Varilrix Group | Prevenar + Infanrix + Havrix and/or Varilrix Group | Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 390 | 30 | 102 | |
| Units: Participants | | | | |
| Anti-PD antibodies, Y1 (N= 390, 30, 102) | 373 | 11 | 71 | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of seropositive subjects for anti protein D (Anti-PD) [Follow-up Period: Persistence analysis in Year 2 (111345 sub-study)]

| End point title | Number of seropositive subjects for anti protein D (Anti-PD) [Follow-up Period: Persistence analysis in Year 2 (111345 sub-study)] |
|---|---|

End point description:

A seropositive subject was a subject whose anti-PD antibody concentration was greater than or equal to (≥) the cut-off value. The seropositivity cut-off for the assay was 100 EL.U/ML.

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

End point timeframe:

At Year 2 (Y2) (post booster vaccination administered in study 10PN-PD-DIT-007)

| End point values | Synflorix + Infanrix + Havrix and/or Varilrix Group | Prevenar + Infanrix + Havrix and/or Varilrix Group | Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 368 | 29 | 96 | |
| Units: Participants | | | | |
| Anti-PD antibodies, Y2 (N= 368, 29, 96) | 340 | 15 | 65 | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of seropositive subjects for anti-protein D (Anti-PD) [Follow-up Period: Persistence Analysis in Year 4 (111347 sub-study)]

| End point title | Number of seropositive subjects for anti-protein D (Anti-PD) [Follow-up Period: Persistence Analysis in Year 4 (111347 sub-study)] |
|---|---|

End point description:

A seropositive subject was a subject whose anti-PD antibody concentration was greater than or equal to (≥) the cut-off value. The seropositivity cut-off for the assay was 100 EL.U/ML.

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

End point timeframe:

At Year 4 (Y4) (post booster vaccination administered in study 10PN-PD-DIT-007)

| **End point values** | Synflorix + Infanrix + Havrix and/or Varilrix Group | Prevenar + Infanrix + Havrix and/or Varilrix Group | Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 261 | 19 | 74 | |
| Units: Participants | | | | |
| Anti-PD antibodies, Y4 (N= 261, 19, 74) | 241 | 12 | 54 | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of seropositive subjects for anti-protein D (Anti-PD) [Follow-up Period: Immunogenicity Analysis in Year 4 (111347 sub-study)]

| End point title | Number of seropositive subjects for anti-protein D (Anti-PD) [Follow-up Period: Immunogenicity Analysis in Year 4 (111347 sub-study)] |
|---|---|

End point description:

A seropositive subject was a subject whose antibody concentration was greater than or equal to (≥) the cut-off value. The seropositivity cut-off for the assay was 100 EL.U/ML.

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

End point timeframe:

For primed groups: At Month 48+7 days after additional dose (D7);For unprimed group: at Day 0 (D0) (Pre-vaccination [PRE]), at Day 7 (D7) post dose 1 (of the 2-dose catch-up vaccination) and at Month 3 (M3) post dose 2 (of the 2-dose catch-up vaccination)

| **End point values** | Synflorix + Infanrix + Havrix and/or Varilrix Group | Prevenar + Infanrix + Havrix and/or Varilrix Group | Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix | Unprimed Group |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 208 | 14 | 54 | 98 |
| Units: Participants | | | | |
| Anti-PD antibodies, PRE (N= 0, 0, 0, 95) | 0 | 0 | 0 | 54 |
| Anti-PD antibodies, D7 (N= 208, 14, 54, 96) | 207 | 14 | 45 | 92 |
| Anti-PD antibodies, M3 (N= 0, 0, 0, 98) | 0 | 0 | 0 | 98 |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of seropositive subjects for anti-vaccine pneumococcal serotypes antibodies [Follow-up Period: Immunogenicity analysis in Year 4 (111347 sub-study)]

| End point title | Number of seropositive subjects for anti-vaccine pneumococcal serotypes antibodies [Follow-up Period: Immunogenicity analysis in Year 4 (111347 sub-study)] |
|---|---|

End point description:

A seropositive subject was a subject whose antibody concentration was greater than or equal to (≥) the cut-off value. Analysis was performed using the 22F-inhibition Enzyme-linked immunosorbent assay (ELISA), using 0.05 microgram per milliliter (µg/mL) as seropositivity cut off.

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

End point timeframe:

For primed groups: At Month 48+7 days after additional dose (D7);For unprimed group: at Day 0 (D0) (Pre-vaccination [PRE]), at Day 7 (D7) post dose 1 (of the 2-dose catch-up vaccination) and at Month 3 (M3) post dose 2 (of the 2-dose catch-up vaccination)

| End point values | Synflorix + Infanrix + Havrix and/or Varilrix Group | Prevenar + Infanrix + Havrix and/or Varilrix Group | Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix | Unprimed Group |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 208 | 14 | 54 | 98 |
| Units: Participants | | | | |
| Anti-1 antibodies, PRE (N= 0, 0, 0, 97) | 0 | 0 | 0 | 69 |
| Anti-1 antibodies, D7 (N= 208, 14, 54, 98) | 207 | 14 | 54 | 97 |
| Anti-1 antibodies, M3 (N= 0, 0, 0, 98) | 0 | 0 | 0 | 98 |
| Anti-4 antibodies, PRE (N= 0, 0, 0, 97) | 0 | 0 | 0 | 29 |
| Anti-4 antibodies, D7 (N= 208, 14, 54, 98) | 208 | 14 | 54 | 98 |
| Anti-4 antibodies, M3 (N= 0, 0, 0, 98) | 0 | 0 | 0 | 98 |
| Anti-5 antibodies, PRE (N= 0, 0, 0, 97) | 0 | 0 | 0 | 72 |
| Anti-5 antibodies, D7 (N= 208, 14, 54, 98) | 207 | 14 | 54 | 98 |
| Anti-5 antibodies, M3 (N= 0, 0, 0, 98) | 0 | 0 | 0 | 98 |
| Anti-6B antibodies, PRE (N= 0, 0, 0, 97) | 0 | 0 | 0 | 77 |
| Anti-6B antibodies, D7 (N= 208, 14, 54, 97) | 207 | 14 | 54 | 94 |
| Anti-6B antibodies, M3 (N= 0, 0, 0, 98) | 0 | 0 | 0 | 98 |
| Anti-7F antibodies, PRE (N= 0, 0, 0, 97) | 0 | 0 | 0 | 64 |
| Anti-7F antibodies, D7 (N= 208, 14, 54, 98) | 208 | 14 | 54 | 98 |
| Anti-7F antibodies, M3 (N= 0, 0, 0, 98) | 0 | 0 | 0 | 98 |
| Anti-9V antibodies, PRE (N= 0, 0, 0, 97) | 0 | 0 | 0 | 67 |
| Anti-9V antibodies, D7 (N= 208, 14, 54, 98) | 208 | 14 | 54 | 94 |
| Anti-9V antibodies, M3 (N= 0, 0, 0, 98) | 0 | 0 | 0 | 98 |
| Anti-14 antibodies, PRE (N= 0, 0, 0, 96) | 0 | 0 | 0 | 90 |
| Anti-14 antibodies, D7 (N= 208, 14, 54, 98) | 208 | 14 | 54 | 97 |

| | | | | |
|---|---|---|---|---|
| Anti-14 antibodies, M3 (N= 0, 0, 0, 98) | 0 | 0 | 0 | 98 |
| Anti-18C antibodies, PRE (N= 0, 0, 0, 96) | 0 | 0 | 0 | 52 |
| Anti-18C antibodies, D7 (N= 208, 14, 54, 98) | 207 | 14 | 54 | 97 |
| Anti-18C antibodies, M3 (N= 0, 0, 0, 98) | 0 | 0 | 0 | 98 |
| Anti-19F antibodies, PRE (N= 0, 0, 0, 96) | 0 | 0 | 0 | 75 |
| Anti-19F antibodies, D7 (N= 208, 14, 54, 98) | 208 | 14 | 54 | 97 |
| Anti-19F antibodies, M3 (N= 0, 0, 0, 98) | 0 | 0 | 0 | 98 |
| Anti-23F antibodies, PRE (N= 0, 0, 0, 97) | 0 | 0 | 0 | 98 |
| Anti-23F antibodies, D7 (N= 208, 14, 54, 98) | 208 | 14 | 54 | 90 |
| Anti-23F antibodies, M3 (N= 0, 0, 0, 98) | 0 | 0 | 0 | 98 |

## Statistical analyses

No statistical analyses for this end point

## Adverse events information

Timeframe for reporting adverse events:

Solicited and Unsolicited AEs: within 4 days and 31 days post Synflorix vaccination in 111347 study for all subjects. Related SAEs: at Year 1 (111345 study), Year 2 up to Year 4 (111346-11347 study). Any SAEs: during the 111347 study vaccination period.

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

## Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 15.1 |

## Reporting groups

| | |
|---|---|
| Reporting group title | Prevenar + Infanrix + Havrix and/or Varilrix Group |

Reporting group description:

This group consisted of subjects vaccinated with Prevenar vaccine in the 10PN-PD-DIT-001 (105553) and 007 (107046) studies. In 105553 study, subjects had been primed with 3 doses of Prevenar vaccine at 2, 3 and 4 months of age co-administered with Infanrix related vaccines. In 107046 study, subjects had received a booster dose at 12-18 months of age of Prevenar vaccine co-administered with Infanrix hexa vaccine. In this study, in the Year 4 111347 study, subjects had received at Month 48 (4 years post Dose 1 in study 105553) one dose of Synflorix vaccine. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix and/or against varicella (a single dose of Varilrix).

| | |
|---|---|
| Reporting group title | Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix |

Reporting group description:

This group consisted of subjects vaccinated with Prevenar and Synflorix vaccines in the 10PN-PD-DIT-001 (105553) and 10PN-PD-DIT-007 (107046) studies. In 105553 study, subjects had been primed with 3 doses Prevenar vaccine at 2, 3 and 4 months of age co-administered with Infanrix related vaccines. In the 107046 study, subjects had received at 12-18 months of age a booster dose of Synflorix vaccine co-administered with Infanrix hexa vaccine. In this study, in the Year 4 (111347 study), subjects had received at Month 48 (4 years post Dose 1 in study 105553) one additional dose of Synflorix vaccine. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix and/or against varicella (a single dose of Varilrix).

| | |
|---|---|
| Reporting group title | Synflorix + Infanrix + Havrix and/or Varilrix Group |

Reporting group description:

This group consisted of subjects primed with Synflorix vaccine in the 10PN-PD-DIT-001 (1105553) and 007 (107046) studies. In 105553 study, subjects had been primed with 3 doses of Synflorix vaccine at 2, 3 and 4 months of age co-administered with Infanrix related vaccines. In 107046 study, subjects had received a booster dose of Synflorix vaccine at 12-18 months of age co-administered with Infanrix hexa vaccine. In this study, in the Year 4 (111347 study), subjects received at Month 48 (4 years post Dose 1 in study 105553) one additional dose of Synflorix vaccine. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix) and/or against varicella (a single dose of Varilrix).

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

Reporting group description:

This group consisted of subjects between, and including, 64-68 months of age at the time of additional vaccination (primed subjects) or dose 1 (unprimed subjects), and for whom the investigator believed that their parents/guardians could and would comply with the requirements of the protocol. Subjects were not previously vaccinated with any pneumococcal vaccine and received 2 doses of Synflorix vaccine at 64-68 and 66-70 months of age (at Day 0 and Month 2). The Unprimed Group was added only in Year 4 of the study.

| Serious adverse events | Prevenar + Infanrix + Havrix and/or Varilrix Group | Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix | Synflorix + Infanrix + Havrix and/or Varilrix Group |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 102 (0.00%) | 1 / 391 (0.26%) |
| number of deaths (all causes) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Infections and infestations | | | |
| Broncopneumonia | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 102 (0.00%) | 1 / 391 (0.26%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| **Serious adverse events** | Unprimed Group | | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Infections and infestations | | | |
| Broncopneumonia | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| **Non-serious adverse events** | Prevenar + Infanrix + Havrix and/or Varilrix Group | Prevenar + Synflorix + Infanrix + Havrix and/or Varilrix | Synflorix + Infanrix + Havrix and/or Varilrix Group |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 12 / 31 (38.71%) | 39 / 102 (38.24%) | 188 / 391 (48.08%) |
| General disorders and administration site conditions | | | |
| Pain | | | |
| subjects affected / exposed[1] | 9 / 20 (45.00%) | 34 / 64 (53.13%) | 157 / 264 (59.47%) |
| occurrences (all) | 9 | 34 | 157 |
| Redness | | | |
| subjects affected / exposed[2] | 5 / 20 (25.00%) | 14 / 64 (21.88%) | 90 / 264 (34.09%) |
| occurrences (all) | 5 | 14 | 90 |
| Swelling | | | |
| subjects affected / exposed[3] | 4 / 20 (20.00%) | 15 / 64 (23.44%) | 67 / 264 (25.38%) |
| occurrences (all) | 4 | 15 | 67 |

| | | | |
|---|---|---|---|
| Drowsiness | | | |
| subjects affected / exposed[4] | 2 / 20 (10.00%) | 12 / 64 (18.75%) | 49 / 263 (18.63%) |
| occurrences (all) | 2 | 12 | 49 |
| Irritability | | | |
| subjects affected / exposed[5] | 4 / 20 (20.00%) | 6 / 64 (9.38%) | 35 / 263 (13.31%) |
| occurrences (all) | 4 | 6 | 35 |
| Loss of appetite | | | |
| subjects affected / exposed[6] | 3 / 20 (15.00%) | 6 / 64 (9.38%) | 30 / 263 (11.41%) |
| occurrences (all) | 3 | 6 | 30 |
| Fever (Axillary temperature ≥ 37.5° C) | | | |
| subjects affected / exposed[7] | 0 / 20 (0.00%) | 2 / 64 (3.13%) | 13 / 263 (4.94%) |
| occurrences (all) | 0 | 2 | 13 |

| **Non-serious adverse events** | Unprimed Group | | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 65 / 100 (65.00%) | | |
| General disorders and administration site conditions | | | |
| Pain | | | |
| subjects affected / exposed[1] | 54 / 100 (54.00%) | | |
| occurrences (all) | 54 | | |
| Redness | | | |
| subjects affected / exposed[2] | 21 / 100 (21.00%) | | |
| occurrences (all) | 21 | | |
| Swelling | | | |
| subjects affected / exposed[3] | 20 / 100 (20.00%) | | |
| occurrences (all) | 20 | | |
| Drowsiness | | | |
| subjects affected / exposed[4] | 12 / 100 (12.00%) | | |
| occurrences (all) | 12 | | |
| Irritability | | | |
| subjects affected / exposed[5] | 8 / 100 (8.00%) | | |
| occurrences (all) | 8 | | |
| Loss of appetite | | | |
| subjects affected / exposed[6] | 13 / 100 (13.00%) | | |
| occurrences (all) | 13 | | |
| Fever (Axillary temperature ≥ 37.5° | | | |

| | | | |
|---|---|---|---|
| C) | | | |
| subjects affected / exposed[7] | 5 / 100 (5.00%) | | |
| occurrences (all) | 5 | | |

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: Analysis for solicited symptoms post vaccination was done solely on subjects participating to the Immunological Memory phase of the 111347 study, on subjects with results available for the specified symptom.

[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: Analysis for solicited symptoms post vaccination was done solely on subjects participating to the Immunological Memory phase of the 111347 study, on subjects with results available for the specified symptom.

[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: Analysis for solicited symptoms post vaccination was done solely on subjects participating to the Immunological Memory phase of the 111347 study, on subjects with results available for the specified symptom.

[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: Analysis for solicited symptoms post vaccination was done solely on subjects participating to the Immunological Memory phase of the 111347 study, on subjects with results available for the specified symptom.

[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Analysis for solicited symptoms post vaccination was done solely on subjects participating to the Immunological Memory phase of the 111347 study, on subjects with results available for the specified symptom.

[6] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Analysis for solicited symptoms post vaccination was done solely on subjects participating to the Immunological Memory phase of the 111347 study, on subjects with results available for the specified symptom.

[7] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Analysis for solicited symptoms post vaccination was done solely on subjects participating to the Immunological Memory phase of the 111347 study, on subjects with results available for the specified symptom.

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 22 June 2010 | Amendment 1<br>Some aspects of study design, endpoints and study conclusion regarding the immunological memory and assessment of immune response following a second-dose of the vaccine have been added for the clarity of the study. |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported