

**Clinical trial results:**

A phase II, randomized, controlled, observer-blind study to evaluate the impact of two formulations of GlaxoSmithKline (GSK) Biologicals' combined 10-valent pneumococcal polysaccharide and non-typeable Haemophilus influenzae protein D conjugate and pneumococcal protein vaccine on nasopharyngeal carriage, safety and immunogenicity when co-administered with routine EPI vaccines in infants following safety assessment in children aged 2-4 years in the Gambia.

Summary

EudraCT number	2012-002727-15
Trial protocol	Outside EU/EEA
Global end of trial date	18 March 2013

Results information

Result version number	v4 (current)
This version publication date	28 February 2019
First version publication date	26 July 2015
Version creation reason	• New data added to full data set Additional immuno results

Trial information**Trial identification**

Sponsor protocol code	114174
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01262872
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline Biologicals
Sponsor organisation address	Rue de l'Institut 89, Rixensart, Belgium, B-1330
Public contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 44 2089904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 44 2089904466, GSKClinicalSupportHD@gsk.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	14 December 2018
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	18 March 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- To assess the safety and reactogenicity of GSK Biologicals' combined Synflorix™(10Pn-PD-DiT) and pneumococcal protein vaccine when administered (high dose formulation [HD]) as a one-dose schedule to children aged 2-4 years, in terms of occurrence of grade 3 related solicited and unsolicited adverse events and related serious adverse events. (Cohort 1, young children)

-To assess the impact of GSK Biologicals' combined Synflorix™(10Pn-PD-DiT) and pneumococcal protein vaccine on nasopharyngeal carriage of non-vaccine S. pneumoniae serotypes when co-administered with routine EPI vaccines as a 3-dose vaccination course (either at 2-3-4 months of age for the low dose (LD) and high dose (HD) formulations or at 2-4-9 months of age for the HD formulation). (Cohort 2, infants)

Note: Routine EPI paediatric immunization in The Gambia includes vaccination against diphtheria, tetanus, pertussis, measles and yellow fever.

Protection of trial subjects:

GSK monitored the study to verify that, amongst others, the data were authentic, accurate, and complete; Safety and rights of subjects were being protected; Study was conducted in accordance with the currently approved protocol and any amendments, any other study agreements, GCP and all applicable regulatory requirements.

The investigator and the head of the medical institution (where applicable) agreed to allow the monitor direct access to all relevant documents.

All subjects were supervised closely for at least 30 minutes following vaccination with appropriate medical treatment readily available. Vaccines were administered by qualified and trained personnel. Vaccines were administered only to eligible subjects that had no contraindications to any components of the vaccines. Subjects were followed-up from the time the subject consents to participate in the study until she/he was discharged.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 February 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Gambia: 1320
Worldwide total number of subjects	1320
EEA total number of subjects	0

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	1200
Children (2-11 years)	120
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:

Cohort 1 subjects participated in Step 1 (duration of about 6 months). Cohort 2 subjects participated in Step 2 (duration of about 10 months). Enrolment for Step 2 was conditional upon successful results of a post-vaccination safety evaluation of all children enrolled in Cohort 1 by an Independent Data Monitoring Committee.

Pre-assignment

Screening details:

During the screening the following steps occurred: check for inclusion/exclusion criteria, contraindications/precautions, medical history of the subjects and signing informed consent forms.

Period 1

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

Blinding implementation details:

Step 1 of the study was conducted in an observer-blind manner. Step 2 was conducted in an observed-blind manner inside each defined vaccination schedule and open between schedules. By observer-blind, it is meant that during the course of the study, the vaccine recipient and those responsible for the evaluation of any study endpoint (e.g., carriage, safety, reactogenicity and immunogenicity) were all unaware of which vaccine was administered.

Arms

Are arms mutually exclusive?	Yes
Arm title	10PP-LD 3+0d Group

Arm description:

This group consisted in infants aged 8-10 weeks at first vaccination enrolled as part the Cohort 2/Step 2 of the study who received 3 doses of the GSK 2189242A (or 10PP) vaccine in its low-dose (LD) formulation and EPI vaccines according to a 3+0 Schedule. That is, subjects received 3 doses of the 10PP vaccine, LD formulation, co-administered with Tritanrix™-HepB/Hib and Polio Sabin™ at 2-3-4 months of age (Day 0, Month 1 and Month 2), followed by one dose of each of the M-Vac™, Stamaril™ and Polio Sabin™ vaccines administered at approximately 9 months of age. The 10PP vaccine was administered intramuscularly into the right thigh; Tritanrix™-HepB/Hib, M-Vac™ and Stamaril™ were administered intramuscularly into the left thigh; Polio Sabin™ was administered orally.

Arm type	Experimental
Investigational medicinal product name	Pneumococcal vaccine GSK 2189242A (LD formulation 1)
Investigational medicinal product code	
Other name	10PP, LD Formulation
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection (IM) into the right thigh.

Investigational medicinal product name	Tritanrix™-HepB/Hib
Investigational medicinal product code	
Other name	DTPw-HBV/Hib
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection (IM) administered into the left thigh.

Investigational medicinal product name	Polio Sabin™
Investigational medicinal product code	
Other name	Oral Polio vaccine (OPV)
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

The vaccine was administered orally.

Investigational medicinal product name	M-Vac™
Investigational medicinal product code	
Other name	Measles
Pharmaceutical forms	Powder and suspension for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

The vaccine was administered into the left thigh.

Investigational medicinal product name	Stamaril™
Investigational medicinal product code	
Other name	Yellow Fever Vaccine (YFV)
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

The vaccine was administered into the left thigh.

Arm title	10PP-HD 3+0d Group
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Arm description:

This group consisted in infants aged 8-10 weeks at first vaccination enrolled as part the Cohort 2/Step 2 of the study who received 3 doses of the GSK 2189242A (or 10PP) vaccine in its high-dose (HD) formulation and EPI vaccines according to a 3+0 Schedule. That is, subjects received 3 doses of the 10PP vaccine, HD formulation, co-administered with the Tritanrix™-HepB/Hib and Polio Sabin™ at 2-3-4 months of age (Day 0, Month 1 and Month 2), followed by one dose of each of the M-Vac™, Stamaril™ and Polio Sabin™ vaccines administered at approximately 9 months of age. The 10PP vaccine was administered intramuscularly into the right thigh; Tritanrix™-HepB/Hib, M-Vac™ and Stamaril™ were administered intramuscularly into the left thigh; Polio Sabin™ was administered orally.

Arm type	Experimental
Investigational medicinal product name	Pneumococcal vaccine GSK 2189242A (HD formulation 2)
Investigational medicinal product code	
Other name	10PP, HD Formulation
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection (IM) into the right thigh.

Investigational medicinal product name	Tritanrix™-HepB/Hib
Investigational medicinal product code	
Other name	DTPw-HBV/Hib
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

The vaccine was administered into the left thigh.

Investigational medicinal product name	Polio Sabin™
Investigational medicinal product code	
Other name	Oral Polio vaccine (OPV)
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

The vaccine was administered orally.

Investigational medicinal product name	M-Vac™
Investigational medicinal product code	
Other name	Measles
Pharmaceutical forms	Powder and suspension for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

The vaccine was administered into the left thigh.

Investigational medicinal product name	Stamaril™
Investigational medicinal product code	
Other name	Yellow Fever Vaccine (YFV)
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

The vaccine was administered into the left thigh.

Arm title	Synflorix 3+0d Group
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Arm description:

This group consisted in infants aged 8-10 weeks at first vaccination enrolled as part the Cohort 2/Step 2 of the study who received 3 doses of Synflorix™ and EPI vaccines according to a 3+0 Schedule. That is, subjects received 3 doses of the Synflorix™, co-administered with Tritanrix™-HepB/Hib and Polio Sabin™ at 2-3-4 months of age (Day 0, Month 1 and Month 2), followed by one dose of each of the M-Vac™, Stamaril™ and Polio Sabin™ vaccines administered at approximately 9 months of age. Synflorix™ was administered intramuscularly into the right thigh; Tritanrix™-HepB/Hib, M-Vac™ and Stamaril™ were administered intramuscularly into the left thigh; Polio Sabin™ was administered orally.

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

Dosage and administration details:

Intramuscular injection (IM) into the right thigh.

Investigational medicinal product name	Tritanrix™-HepB/Hib
Investigational medicinal product code	
Other name	DTPw-HBV/Hib
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

The vaccine was administered into the left thigh.

Investigational medicinal product name	Polio Sabin™
Investigational medicinal product code	
Other name	Oral Polio vaccine (OPV)
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

The vaccine was administered orally.

Investigational medicinal product name	M-Vac™
Investigational medicinal product code	
Other name	Measles
Pharmaceutical forms	Powder and suspension for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

The vaccine was administered into the left thigh.

Investigational medicinal product name	Stamaril™
Investigational medicinal product code	
Other name	Yellow Fever Vaccine (YFV)
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
The vaccine was administered into the left thigh.	
Arm title	Prevnar13 3+0d Group
Arm description:	
This group consisted in infants aged 8-10 weeks at first vaccination enrolled as part the Cohort 2/Step 2 of the study who received 3 doses of Prevnar 13™ and EPI vaccines according to a 3+0 Schedule. That is, subjects received 3 doses of Prevnar 13™, co-administered with Tritanrix™-HepB/Hib and Polio Sabin™ at 2-3-4 months of age (Day 0, Month 1 and Month 2), followed by one dose of each of the M-Vac™, Stamaril™ and Polio Sabin™ vaccines administered at approximately 9 months of age. Prevnar 13™ was administered intramuscularly into the right thigh; Tritanrix™-HepB/Hib, M-Vac™ and Stamaril™ were administered intramuscularly into the left thigh; Polio Sabin™ was administered orally.	
Arm type	Active comparator
Investigational medicinal product name	Prevnar13™
Investigational medicinal product code	
Other name	Prev13
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
Intramuscular injection (IM) into the right thigh.	
Investigational medicinal product name	Tritanrix™-HepB/Hib
Investigational medicinal product code	
Other name	DTPw-HBV/Hib
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
The vaccine was administered into the left thigh.	
Investigational medicinal product name	Polio Sabin™
Investigational medicinal product code	
Other name	Oral Polio vaccine (OPV)
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use
Dosage and administration details:	
The vaccine was administered orally.	
Investigational medicinal product name	M-Vac™
Investigational medicinal product code	
Other name	Measles
Pharmaceutical forms	Powder and suspension for suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
The vaccine was administered into the left thigh.	
Investigational medicinal product name	Stamaril™
Investigational medicinal product code	
Other name	Yellow Fever Vaccine (YFV)
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
The vaccine was administered into the left thigh.	
Arm title	10PP-HD 2+1d Group

Arm description:

This group consisted in infants aged 8-10 weeks at first vaccination enrolled as part the Cohort 2/Step 2 of the study who received the GSK 2189242A (or 10PP) vaccine, in its high-dose (HD) formulation, and EPI vaccines according to a 2+1 Schedule. That is, subjects received 2 doses of the 10PP vaccine, HD formulation co-administered with Tritanrix™-Hep B/Hib and Polio Sabin™ at 2-4 months of age (at Day 0 and Month 2), followed by a third dose of the same formulation co-administered with M-Vac™, Stamaril™ and Polio Sabin™ at approximately 9 months of age.. The 2nd doses of Tritanrix™-Hep B/Hib and Polio Sabin™ in EPI vaccines were administered without any pneumococcal vaccine at 3 months of age. The 10PP vaccine was administered intramuscularly into the right thigh; Tritanrix™-HepB/Hib, M-Vac™ and Stamaril™ were administered intramuscularly into the left thigh; Polio Sabin™ was administered orally.

Arm type	Experimental
Investigational medicinal product name	Pneumococcal vaccine GSK 2189242A (HD formulation 2)
Investigational medicinal product code	
Other name	10PP, HD Formulation
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection (IM) into the right thigh.

Investigational medicinal product name	Tritanrix™-HepB/Hib
Investigational medicinal product code	
Other name	DTPw-HBV/Hib
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

The vaccine was administered into the left thigh.

Investigational medicinal product name	Polio Sabin™
Investigational medicinal product code	
Other name	Oral Polio vaccine (OPV)
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

The vaccine was administered orally.

Investigational medicinal product name	M-Vac™
Investigational medicinal product code	
Other name	Measles
Pharmaceutical forms	Powder and suspension for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

The vaccine was administered into the left thigh.

Investigational medicinal product name	Stamaril™
Investigational medicinal product code	
Other name	Yellow Fever Vaccine (YFV)
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

The vaccine was administered into the left thigh.

Arm title	Synflorix 2+1d Group
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Arm description:

This group consisted in infants aged 8-10 weeks at first vaccination enrolled as part the Cohort 2/Step 2 of the study who received Synflorix™ and EPI vaccines according to a 2+1 Schedule. That is, subjects received 2 doses of the Synflorix™ co-administered with Tritanrix™-Hep B/Hib and Polio Sabin™ at 2-4 months of age (at Day 0 and Month 2), followed by a third dose of Synflorix™ co-administered with M-Vac™, Stamaril™ and Polio Sabin™ at approximately 9 months of age. The 2nd doses of Tritanrix™-Hep B/Hib and Polio Sabin™ in EPI vaccines were administered without any pneumococcal vaccine at 3

months of age. Synflorix™ was administered intramuscularly into the right thigh; Tritanrix™-HepB/Hib, M-Vac™ and Stamaril™ were administered intramuscularly into the left thigh; Polio Sabin™ was administered orally.

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

Dosage and administration details:

Intramuscular injection (IM) into the right thigh.

Investigational medicinal product name	Tritanrix™-HepB/Hib
Investigational medicinal product code	
Other name	DTPw-HBV/Hib
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

The vaccine was administered into the left thigh.

Investigational medicinal product name	Polio Sabin™
Investigational medicinal product code	
Other name	Oral Polio vaccine (OPV)
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

The vaccine was administered orally.

Investigational medicinal product name	M-Vac™
Investigational medicinal product code	
Other name	Measles
Pharmaceutical forms	Powder and suspension for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

The vaccine was administered into the left thigh.

Investigational medicinal product name	Stamaril™
Investigational medicinal product code	
Other name	Yellow Fever Vaccine (YFV)
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

The vaccine was administered into the left thigh.

Arm title	10PP-HD 1d Group
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Arm description:

This group consisted in children aged 2-4 years at vaccination enrolled as part of the Cohort 1/Step 1 of the study who received a single dose of the GSK 2189242A (or 10PP) vaccine in its high-dose (HD) formulation at Day 0. The 10PP vaccine was administered intramuscularly in the non-dominant deltoid.

Arm type	Experimental
Investigational medicinal product name	Pneumococcal vaccine GSK 2189242A (LD formulation 1)
Investigational medicinal product code	
Other name	10PP, LD Formulation
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection (IM) into the deltoid region of the non-dominant arm.

Arm title	Prevnar13 1d Group
Arm description:	
This group consisted in children aged 2-4 years at vaccination enrolled as part of the Cohort 1/Step 1 of the study who received a single dose of Prevnar 13™ at Day 0. Prevnar 13™ was administered intramuscularly in the non-dominant deltoid.	
Arm type	Active comparator
Investigational medicinal product name	Prevnar13™
Investigational medicinal product code	
Other name	Prev13
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection (IM) into the deltoid region of the non-dominant arm.

Number of subjects in period 1	10PP-LD 3+0d Group	10PP-HD 3+0d Group	Synflorix 3+0d Group
Started	200	200	200
Completed	191	190	195
Not completed	9	10	5
Adverse event, serious fatal	-	1	-
Consent withdrawn by subject	4	6	3
Migrated/moved from study area	4	3	2
Protocol deviation	1	-	-

Number of subjects in period 1	Prevnar13 3+0d Group	10PP-HD 2+1d Group	Synflorix 2+1d Group
Started	200	200	200
Completed	191	191	194
Not completed	9	9	6
Adverse event, serious fatal	2	2	1
Consent withdrawn by subject	1	2	1
Migrated/moved from study area	6	2	3
Protocol deviation	-	3	1

Number of subjects in period 1	10PP-HD 1d Group	Prevnar13 1d Group
Started	60	60
Completed	60	60
Not completed	0	0
Adverse event, serious fatal	-	-
Consent withdrawn by subject	-	-
Migrated/moved from study area	-	-
Protocol deviation	-	-

Baseline characteristics

Reporting groups

Reporting group title	10PP-LD 3+0d Group
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Reporting group description:

This group consisted in infants aged 8-10 weeks at first vaccination enrolled as part the Cohort 2/Step 2 of the study who received 3 doses of the GSK 2189242A (or 10PP) vaccine in its low-dose (LD) formulation and EPI vaccines according to a 3+0 Schedule. That is, subjects received 3 doses of the 10PP vaccine, LD formulation, co-administered with Tritanrix™-HepB/Hib and Polio Sabin™ at 2-3-4 months of age (Day 0, Month 1 and Month 2), followed by one dose of each of the M-Vac™, Stamaril™ and Polio Sabin™ vaccines administered at approximately 9 months of age. The 10PP vaccine was administered intramuscularly into the right thigh; Tritanrix™-HepB/Hib, M-Vac™ and Stamaril™ were administered intramuscularly into the left thigh; Polio Sabin™ was administered orally.

Reporting group title	10PP-HD 3+0d Group
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Reporting group description:

This group consisted in infants aged 8-10 weeks at first vaccination enrolled as part the Cohort 2/Step 2 of the study who received 3 doses of the GSK 2189242A (or 10PP) vaccine in its high-dose (HD) formulation and EPI vaccines according to a 3+0 Schedule. That is, subjects received 3 doses of the 10PP vaccine, HD formulation, co-administered with the Tritanrix™-HepB/Hib and Polio Sabin™ at 2-3-4 months of age (Day 0, Month 1 and Month 2), followed by one dose of each of the M-Vac™, Stamaril™ and Polio Sabin™ vaccines administered at approximately 9 months of age. The 10PP vaccine was administered intramuscularly into the right thigh; Tritanrix™-HepB/Hib, M-Vac™ and Stamaril™ were administered intramuscularly into the left thigh; Polio Sabin™ was administered orally.

Reporting group title	Synflorix 3+0d Group
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Reporting group description:

This group consisted in infants aged 8-10 weeks at first vaccination enrolled as part the Cohort 2/Step 2 of the study who received 3 doses of Synflorix™ and EPI vaccines according to a 3+0 Schedule. That is, subjects received 3 doses of the Synflorix™, co-administered with Tritanrix™-HepB/Hib and Polio Sabin™ at 2-3-4 months of age (Day 0, Month 1 and Month 2), followed by one dose of each of the M-Vac™, Stamaril™ and Polio Sabin™ vaccines administered at approximately 9 months of age. Synflorix™ was administered intramuscularly into the right thigh; Tritanrix™-HepB/Hib, M-Vac™ and Stamaril™ were administered intramuscularly into the left thigh; Polio Sabin™ was administered orally.

Reporting group title	Prevnar13 3+0d Group
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Reporting group description:

This group consisted in infants aged 8-10 weeks at first vaccination enrolled as part the Cohort 2/Step 2 of the study who received 3 doses of Prevnar 13™ and EPI vaccines according to a 3+0 Schedule. That is, subjects received 3 doses of Prevnar 13™, co-administered with Tritanrix™-HepB/Hib and Polio Sabin™ at 2-3-4 months of age (Day 0, Month 1 and Month 2), followed by one dose of each of the M-Vac™, Stamaril™ and Polio Sabin™ vaccines administered at approximately 9 months of age. Prevnar 13™ was administered intramuscularly into the right thigh; Tritanrix™-HepB/Hib, M-Vac™ and Stamaril™ were administered intramuscularly into the left thigh; Polio Sabin™ was administered orally.

Reporting group title	10PP-HD 2+1d Group
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Reporting group description:

This group consisted in infants aged 8-10 weeks at first vaccination enrolled as part the Cohort 2/Step 2 of the study who received the GSK 2189242A (or 10PP) vaccine, in its high-dose (HD) formulation, and EPI vaccines according to a 2+1 Schedule. That is, subjects received 2 doses of the 10PP vaccine, HD formulation co-administered with Tritanrix™-Hep B/Hib and Polio Sabin™ at 2-4 months of age (at Day 0 and Month 2), followed by a third dose of the same formulation co-administered with M-Vac™, Stamaril™ and Polio Sabin™ at approximately 9 months of age.. The 2nd doses of Tritanrix™-Hep B/Hib and Polio Sabin™ in EPI vaccines were administered without any pneumococcal vaccine at 3 months of age. The 10PP vaccine was administered intramuscularly into the right thigh; Tritanrix™-HepB/Hib, M-Vac™ and Stamaril™ were administered intramuscularly into the left thigh; Polio Sabin™ was administered orally.

Reporting group title	Synflorix 2+1d Group
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Reporting group description:

This group consisted in infants aged 8-10 weeks at first vaccination enrolled as part the Cohort 2/Step 2 of the study who received Synflorix™ and EPI vaccines according to a 2+1 Schedule. That is, subjects received 2 doses of the Synflorix™ co-administered with Tritanrix™-Hep B/Hib and Polio Sabin™ at 2-4 months of age (at Day 0 and Month 2), followed by a third dose of Synflorix™ co-administered with M-Vac™, Stamaril™ and Polio Sabin™ at approximately 9 months of age. The 2nd doses of Tritanrix™-Hep B/Hib and Polio Sabin™ in EPI vaccines were administered without any pneumococcal vaccine at 3 months of age. Synflorix™ was administered intramuscularly into the right thigh; Tritanrix™-HepB/Hib,

M-Vac™ and Stamaril™ were administered intramuscularly into the left thigh; Polio Sabin™ was administered orally.

Reporting group title	10PP-HD 1d Group
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Reporting group description:

This group consisted in children aged 2-4 years at vaccination enrolled as part of the Cohort 1/Step 1 of the study who received a single dose of the GSK 2189242A (or 10PP) vaccine in its high-dose (HD) formulation at Day 0. The 10PP vaccine was administered intramuscularly in the non-dominant deltoid.

Reporting group title	Prevnar13 1d Group
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Reporting group description:

This group consisted in children aged 2-4 years at vaccination enrolled as part of the Cohort 1/Step 1 of the study who received a single dose of Prevnar 13™ at Day 0. Prevnar 13™ was administered intramuscularly in the non-dominant deltoid.

Reporting group values	10PP-LD 3+0d Group	10PP-HD 3+0d Group	Synflorix 3+0d Group
Number of subjects	200	200	200
Age categorical Units: Subjects			
Infants and toddlers (28 days-23 months)	200	200	200
Children (2-11 years)	0	0	0
Gender categorical Units: Subjects			
Female	105	98	103
Male	95	102	97

Reporting group values	Prevnar13 3+0d Group	10PP-HD 2+1d Group	Synflorix 2+1d Group
Number of subjects	200	200	200
Age categorical Units: Subjects			
Infants and toddlers (28 days-23 months)	200	200	200
Children (2-11 years)	0	0	0
Gender categorical Units: Subjects			
Female	103	103	97
Male	97	97	103

Reporting group values	10PP-HD 1d Group	Prevnar13 1d Group	Total
Number of subjects	60	60	1320
Age categorical Units: Subjects			
Infants and toddlers (28 days-23 months)	0	0	1200
Children (2-11 years)	60	60	120
Gender categorical Units: Subjects			
Female	41	26	676
Male	19	34	644

End points

End points reporting groups

Reporting group title	10PP-LD 3+0d Group
Reporting group description:	
This group consisted in infants aged 8-10 weeks at first vaccination enrolled as part the Cohort 2/Step 2 of the study who received 3 doses of the GSK 2189242A (or 10PP) vaccine in its low-dose (LD) formulation and EPI vaccines according to a 3+0 Schedule. That is, subjects received 3 doses of the 10PP vaccine, LD formulation, co-administered with Tritanrix™-HepB/Hib and Polio Sabin™ at 2-3-4 months of age (Day 0, Month 1 and Month 2), followed by one dose of each of the M-Vac™, Stamaril™ and Polio Sabin™ vaccines administered at approximately 9 months of age. The 10PP vaccine was administered intramuscularly into the right thigh; Tritanrix™-HepB/Hib, M-Vac™ and Stamaril™ were administered intramuscularly into the left thigh; Polio Sabin™ was administered orally.	
Reporting group title	10PP-HD 3+0d Group
Reporting group description:	
This group consisted in infants aged 8-10 weeks at first vaccination enrolled as part the Cohort 2/Step 2 of the study who received 3 doses of the GSK 2189242A (or 10PP) vaccine in its high-dose (HD) formulation and EPI vaccines according to a 3+0 Schedule. That is, subjects received 3 doses of the 10PP vaccine, HD formulation, co-administered with the Tritanrix™-HepB/Hib and Polio Sabin™ at 2-3-4 months of age (Day 0, Month 1 and Month 2), followed by one dose of each of the M-Vac™, Stamaril™ and Polio Sabin™ vaccines administered at approximately 9 months of age. The 10PP vaccine was administered intramuscularly into the right thigh; Tritanrix™-HepB/Hib, M-Vac™ and Stamaril™ were administered intramuscularly into the left thigh; Polio Sabin™ was administered orally.	
Reporting group title	Synflorix 3+0d Group
Reporting group description:	
This group consisted in infants aged 8-10 weeks at first vaccination enrolled as part the Cohort 2/Step 2 of the study who received 3 doses of Synflorix™ and EPI vaccines according to a 3+0 Schedule. That is, subjects received 3 doses of the Synflorix™, co-administered with Tritanrix™-HepB/Hib and Polio Sabin™ at 2-3-4 months of age (Day 0, Month 1 and Month 2), followed by one dose of each of the M-Vac™, Stamaril™ and Polio Sabin™ vaccines administered at approximately 9 months of age. Synflorix™ was administered intramuscularly into the right thigh; Tritanrix™-HepB/Hib, M-Vac™ and Stamaril™ were administered intramuscularly into the left thigh; Polio Sabin™ was administered orally.	
Reporting group title	Prevnar13 3+0d Group
Reporting group description:	
This group consisted in infants aged 8-10 weeks at first vaccination enrolled as part the Cohort 2/Step 2 of the study who received 3 doses of Prevnar 13™ and EPI vaccines according to a 3+0 Schedule. That is, subjects received 3 doses of Prevnar 13™, co-administered with Tritanrix™-HepB/Hib and Polio Sabin™ at 2-3-4 months of age (Day 0, Month 1 and Month 2), followed by one dose of each of the M-Vac™, Stamaril™ and Polio Sabin™ vaccines administered at approximately 9 months of age. Prevnar 13™ was administered intramuscularly into the right thigh; Tritanrix™-HepB/Hib, M-Vac™ and Stamaril™ were administered intramuscularly into the left thigh; Polio Sabin™ was administered orally.	
Reporting group title	10PP-HD 2+1d Group
Reporting group description:	
This group consisted in infants aged 8-10 weeks at first vaccination enrolled as part the Cohort 2/Step 2 of the study who received the GSK 2189242A (or 10PP) vaccine, in its high-dose (HD) formulation, and EPI vaccines according to a 2+1 Schedule. That is, subjects received 2 doses of the 10PP vaccine, HD formulation co-administered with Tritanrix™-Hep B/Hib and Polio Sabin™ at 2-4 months of age (at Day 0 and Month 2), followed by a third dose of the same formulation co-administered with M-Vac™, Stamaril™ and Polio Sabin™ at approximately 9 months of age.. The 2nd doses of Tritanrix™-Hep B/Hib and Polio Sabin™ in EPI vaccines were administered without any pneumococcal vaccine at 3 months of age. The 10PP vaccine was administered intramuscularly into the right thigh; Tritanrix™-HepB/Hib, M-Vac™ and Stamaril™ were administered intramuscularly into the left thigh; Polio Sabin™ was administered orally.	
Reporting group title	Synflorix 2+1d Group
Reporting group description:	
This group consisted in infants aged 8-10 weeks at first vaccination enrolled as part the Cohort 2/Step 2 of the study who received Synflorix™ and EPI vaccines according to a 2+1 Schedule. That is, subjects received 2 doses of the Synflorix™ co-administered with Tritanrix™-Hep B/Hib and Polio Sabin™ at 2-4 months of age (at Day 0 and Month 2), followed by a third dose of Synflorix™ co-administered with M-Vac™, Stamaril™ and Polio Sabin™ at approximately 9 months of age. The 2nd doses of Tritanrix™-Hep B/Hib and Polio Sabin™ in EPI vaccines were administered without any pneumococcal vaccine at 3 months of age. Synflorix™ was administered intramuscularly into the right thigh; Tritanrix™-HepB/Hib,	

M-Vac™ and Stamaril™ were administered intramuscularly into the left thigh; Polio Sabin™ was administered orally.

Reporting group title	10PP-HD 1d Group
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Reporting group description:

This group consisted in children aged 2-4 years at vaccination enrolled as part of the Cohort 1/Step 1 of the study who received a single dose of the GSK 2189242A (or 10PP) vaccine in its high-dose (HD) formulation at Day 0. The 10PP vaccine was administered intramuscularly in the non-dominant deltoid.

Reporting group title	Prevnam13 1d Group
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Reporting group description:

This group consisted in children aged 2-4 years at vaccination enrolled as part of the Cohort 1/Step 1 of the study who received a single dose of Prevnam 13™ at Day 0. Prevnam 13™ was administered intramuscularly in the non-dominant deltoid.

Subject analysis set title	Total "all 5" Group
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Subject analysis set type	Sub-group analysis
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Subject analysis set description:

A subset of samples selected for ply and phtD gene sequencing of *S. pneumoniae* isolates, isolated from nasopharyngeal samples across all time points and across study groups of Cohort 2 (Prev13_3 group was excluded).

Primary: Number of subjects with any and Grade 3 solicited local symptoms and Grade 3 solicited local symptoms with relationship to vaccination – For Step 1/Cohort 1 subjects

End point title	Number of subjects with any and Grade 3 solicited local symptoms and Grade 3 solicited local symptoms with relationship to vaccination – For Step 1/Cohort 1 subjects ^{[1][2]}
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End point description:

Assessed local symptoms were pain, redness and swelling. Any = Occurrence of the specified solicited local symptom, regardless of intensity. Grade 3 Pain = Crying when limb was moved/spontaneously painful. Grade 3 Redness/Swelling = Redness/swelling at injection site larger than (>) 30 millimeters (mm). All solicited local symptoms were systematically considered by the investigators as causally related to vaccination. Primary results correspond to results for occurrences of Grade 3 symptoms. This outcome concerns subjects enrolled in Cohort 1/Step 1.

End point type	Primary
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End point timeframe:

Within the 4-day (Days 0-3) period post vaccination with pneumococcal vaccine (10PP vaccine or Prevnam 13™)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The scope of this primary end point was descriptive, no statistical hypothesis test was performed.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1. Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-HD 1d Group	Prevnam13 1d Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	60		
Units: Subjects				
Any Pain	0	0		
Grade 3 Pain	0	0		
Any Redness	0	0		
Grade 3 Redness	0	0		
Any Swelling	1	0		
Grade 3 Swelling	1	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with any and Grade 3 solicited general symptoms with and without relationship to vaccination – For Step 1/Cohort 1 subjects

End point title	Number of subjects with any and Grade 3 solicited general symptoms with and without relationship to vaccination – For Step 1/Cohort 1 subjects ^{[3][4]}
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End point description:

Assessed solicited general symptoms were Drowsiness, Fever (axillary temperature higher than \geq 37.5 degrees Celsius [$^{\circ}$ C]), Irritability/Fussiness and Loss of appetite. Any = Occurrence of the specified solicited general symptom, regardless of intensity and relationship to vaccination. Related = Occurrence of the specified symptom assessed by the investigator as causally related to vaccination. Grade 3 Drowsiness = Drowsiness that prevented normal activity. Grade 3 Fever = Axillary temperature higher than ($>$) 39.5 $^{\circ}$ C. Grade 3 Irritability/fussiness = Crying that could not be comforted/prevented normal activity. Grade 3 Loss of appetite = Subject did not eat at all. Primary results correspond to results for occurrences of Grade 3 symptoms assessed as related to vaccination. This outcome concerns subjects enrolled in Cohort 1/Step 1.

End point type	Primary
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End point timeframe:

Within the 4-day (Days 0-3) period post vaccination with pneumococcal vaccine (10PP vaccine or Prevnar 13TM)

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 scope of this primary end point was descriptive, no statistical hypothesis test was performed.

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1. Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-HD 1d Group	Prevnar13 1d Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	60		
Units: Subjects				
Any Drowsiness	0	0		
Grade 3 Drowsiness	0	0		
Related Drowsiness	0	0		
Grade 3 & Related Drowsiness	0	0		
Any Fever	4	2		
Grade 3 Fever	0	0		
Related Fever	1	1		
Grade 3 & Related Fever	0	0		
Any Irritability/Fussiness	0	0		
Grade 3 Irritability/Fussiness	0	0		
Related Irritability/Fussiness	0	0		
Grade 3 & Related Irritability/Fussiness	0	0		

Any Loss of appetite	1	0		
Grade 3 Loss of appetite	0	0		
Related Loss of appetite	0	0		
Grade 3 & Related Loss of appetite	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with any and Grade 3 unsolicited adverse events (AEs) with and without relationship to vaccination - For Step 1/Cohort 1 subjects

End point title	Number of subjects with any and Grade 3 unsolicited adverse events (AEs) with and without relationship to vaccination - For Step 1/Cohort 1 subjects ^{[5][6]}
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End point description:

An unsolicited 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. An AE can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a medicinal product. For marketed medicinal products, this also includes failure to produce expected benefits (i.e. lack of efficacy), abuse or misuse. Any = Occurrence of AE, regardless of intensity or relationship to vaccination. Grade 3 = Occurrence of AE which prevented normal activities. Related = Occurrence of AE assessed by the investigator as causally related to vaccination. Primary results correspond to results for occurrences of Grade 3 unsolicited AE(s) assessed as related to vaccination. This outcome concerns subjects enrolled in Cohort 1/Step 1.

End point type	Primary
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End point timeframe:

Within the 31-day (Days 0-30) period post vaccination with pneumococcal vaccine (10PP vaccine or Prevnar 13™)

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The scope of this primary end point was descriptive, no statistical hypothesis test was performed.

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-HD 1d Group	Prevnar13 1d Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	60		
Units: Subjects				
Any unsolicited AE(s)	13	7		
Grade 3 unsolicited AE(s)	0	0		
Related unsolicited AE(s)	0	0		
Grade 3 and related unsolicited AE(s)	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with any serious adverse events (SAEs) and with SAE(s) with relationship to vaccination - For Step 1/Cohort 1 subjects

End point title	Number of subjects with any serious adverse events (SAEs) and with SAE(s) with relationship to vaccination - For Step 1/Cohort 1 subjects ^{[7][8]}
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End point description:

SAEs assessed include medical occurrences that result in death, are life threatening, require hospitalization or prolongation of hospitalization, result in disability/incapacity. These should also be considered serious: invasive or malignant cancers, intensive treatment in an emergency room or at home for allergic bronchospasm, blood dyscrasias or convulsions that do not result in hospitalisation. Any = Occurrence of an SAE, regardless of relationship to vaccination. Related = Occurrence of an SAE assessed by the investigator as causally related to vaccination. Primary results correspond to results for occurrences of SAE(s) assessed as related to vaccination. This outcome concerns subjects enrolled in Cohort 1/Step 1.

End point type	Primary
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End point timeframe:

From Day 0 to Month 1

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The scope of this primary end point was descriptive, no statistical hypothesis test was performed.

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1. Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-HD 1d Group	Pprevnar13 1d Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	60		
Units: Subjects				
Any SAE(s)	0	0		
SAE(s) related to vaccination	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with non-vaccine serotypes of Streptococcus pneumoniae (S. pn.) in the nasopharynx – For Cohort 2/Step 2, subjects receiving the 3+0 Schedule

End point title	Number of subjects with non-vaccine serotypes of Streptococcus pneumoniae (S. pn.) in the nasopharynx – For Cohort 2/Step 2, subjects receiving the 3+0 Schedule ^[9]
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End point description:

Any serotype belonging to the same serogroup as the serotypes of the pneumococcal vaccine administered (10PP vaccine, or Synflorix™), but different from 10 vaccine pneumococcal serotypes, was considered for this analysis of carriage. Serotypes were identified through cultures and serotyping of the isolates.

End point type	Primary
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End point timeframe:

At 1, 5 and 8 months (Mth) post-Dose 3 of pneumococcal vaccine administered (10PP vaccine, or Synflorix™)

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-LD 3+0d Group	10PP-HD 3+0d Group	Synflorix 3+0d Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	193	194	196	
Units: Subjects				
1 Mth post dose 3 (N=193, 194, 196)	154	137	145	
5 Mth post dose 3 (N=193, 192, 194)	148	149	159	
8 Mth post dose 3 (N=189, 189, 194)	151	154	159	

Statistical analyses

Statistical analysis title	VE-10PP-LD 3+0d vs Synflorix 3+0d- 1M post-Dose3
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Statistical analysis description:

The analysis aimed to compare occurrences in terms of percentage of subjects with positive nasopharyngeal sample out of the number of subjects with swabs cultured, between 2 groups, one month (M) post-dose 3 of pneumococcal vaccine administered (10PP vaccine or Synflorix™). Vaccine Efficacy (VE) was calculated as 1 minus Relative Risk (i.e. investigational vaccine over control vaccine))*100].

Comparison groups	10PP-LD 3+0d Group v Synflorix 3+0d Group
Number of subjects included in analysis	389
Analysis specification	Pre-specified
Analysis type	equivalence
Parameter estimate	VE
Point estimate	-7.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-36.3
upper limit	14.6

Statistical analysis title	VE-10PP-LD 3+0d vs Synflorix 3+0d- 5M post-Dose3
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Statistical analysis description:

The analysis aimed to compare occurrences in terms of percentage of subjects with positive nasopharyngeal sample out of the number of subjects with swabs cultured, between 2 groups, five months (M) post-dose 3 of pneumococcal vaccine administered (10PP vaccine or Synflorix™). Vaccine Efficacy (VE) was calculated as 1 minus Relative Risk (i.e. investigational vaccine over control vaccine))*100].

Comparison groups	10PP-LD 3+0d Group v Synflorix 3+0d Group
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Number of subjects included in analysis	389
Analysis specification	Pre-specified
Analysis type	equivalence
Parameter estimate	VE
Point estimate	6.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-17.8
upper limit	25.7

Statistical analysis title	VE-10PP-LD 3+0d vs Synflorix 3+0d- 8M post-Dose3
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Statistical analysis description:

The analysis aimed to compare occurrences in terms of percentage of subjects with positive nasopharyngeal sample out of the number of subjects with swabs cultured, between 2 groups, eight months (M) post-dose 3 of pneumococcal vaccine administered (10PP vaccine or Synflorix™). Vaccine Efficacy (VE) was calculated as 1 minus Relative Risk (i.e. investigational vaccine over control vaccine))*100].

Comparison groups	10PP-LD 3+0d Group v Synflorix 3+0d Group
Number of subjects included in analysis	389
Analysis specification	Pre-specified
Analysis type	equivalence
Parameter estimate	VE
Point estimate	2.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-22.6
upper limit	22.5

Statistical analysis title	VE-10PP-HD 3+0d vs Synflorix 3+0d- 1M post-Dose3
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Statistical analysis description:

The analysis aimed to compare occurrences in terms of percentage of subjects with positive nasopharyngeal sample out of the number of subjects with swabs cultured, between 2 groups, one month (M) post-dose 3 of pneumococcal vaccine administered (10PP vaccine or Synflorix™). Vaccine Efficacy (VE) was calculated as 1 minus Relative Risk (i.e. investigational vaccine over control vaccine))*100].

Comparison groups	Synflorix 3+0d Group v 10PP-HD 3+0d Group
Number of subjects included in analysis	390
Analysis specification	Pre-specified
Analysis type	equivalence
Parameter estimate	VE
Point estimate	4.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-21.4
upper limit	25

Statistical analysis title	VE-10PP-HD 3+0d vs Synflorix 3+0d- 5M post-Dose3
Statistical analysis description:	
The analysis aimed to compare occurrences in terms of percentage of subjects with positive nasopharyngeal sample out of the number of subjects with swabs cultured, between 2 groups, five months (M) post-dose 3 of pneumococcal vaccine administered (10PP vaccine or Synflorix™). Vaccine Efficacy (VE) was calculated as 1 minus Relative Risk (i.e. investigational vaccine over control vaccine))*100].	
Comparison groups	10PP-HD 3+0d Group v Synflorix 3+0d Group
Number of subjects included in analysis	390
Analysis specification	Pre-specified
Analysis type	equivalence
Parameter estimate	VE
Point estimate	5.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-19.2
upper limit	24.8

Statistical analysis title	VE-10PP-HD 3+0d vs Synflorix 3+0d- 8M post-Dose3
Statistical analysis description:	
The analysis aimed to compare occurrences in terms of percentage of subjects with positive nasopharyngeal sample out of the number of subjects with swabs cultured, between 2 groups, eight months (M) post-dose 3 of pneumococcal vaccine administered (10PP vaccine or Synflorix™). Vaccine Efficacy (VE) was calculated as 1 minus Relative Risk (i.e. investigational vaccine over control vaccine))*100].	
Comparison groups	10PP-HD 3+0d Group v Synflorix 3+0d Group
Number of subjects included in analysis	390
Analysis specification	Pre-specified
Analysis type	equivalence
Parameter estimate	VE
Point estimate	0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-24.9
upper limit	20.9

Primary: Number of subjects with non-vaccine serotypes of Streptococcus pneumoniae (S. pn.) in the nasopharynx – For Cohort 2/Step 2, subjects receiving the 2+1 Schedule

End point title	Number of subjects with non-vaccine serotypes of Streptococcus pneumoniae (S. pn.) in the nasopharynx – For Cohort 2/Step 2, subjects receiving the 2+1 Schedule ^[10]
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End point description:

Any serotype belonging to the same serogroup as the serotypes of the pneumococcal vaccine

administered (10PP vaccine or Synflorix™), but different from 10 vaccine pneumococcal serotypes, was considered for this analysis of carriage. Serotypes were identified through cultures and serotyping of the isolates.

End point type	Primary
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End point timeframe:

At 1 and 5 months (Mth) post-Dose 2, and at 3 months post-Dose 3 of the pneumococcal vaccine administered (10PP vaccine or Synflorix™)

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-HD 2+1d Group	Synflorix 2+1d Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	197	197		
Units: Subjects				
1 Mth post dose 2 (N=197, 197)	142	152		
5 Mth post dose 2 (N=189, 194)	146	160		
3 Mth post dose 3 (N=190, 193)	165	162		

Statistical analyses

Statistical analysis title	VE-10PP-HD 2+1d vs Synflorix 2+1d- 1M post-Dose2
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Statistical analysis description:

The analysis aimed to compare occurrences in terms of percentage of subjects with positive nasopharyngeal sample out of the number of subjects with swabs cultured, between 2 groups, one month (M) post-dose 2 of pneumococcal vaccine administered (10PP vaccine or Synflorix™). Vaccine Efficacy (VE) was calculated as 1 minus Relative Risk (i.e. investigational vaccine over control vaccine))*100].

Comparison groups	10PP-HD 2+1d Group v Synflorix 2+1d Group
Number of subjects included in analysis	394
Analysis specification	Pre-specified
Analysis type	equivalence
Parameter estimate	VE
Point estimate	6.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-18.2
upper limit	26.2

Statistical analysis title	VE-10PP-HD 2+1d vs Synflorix 2+1d- 5M post-Dose2
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Statistical analysis description:

The analysis aimed to compare occurrences in terms of percentage of subjects with positive nasopharyngeal sample out of the number of subjects with swabs cultured, between 2 groups, five months (M) post-dose 2 of pneumococcal vaccine administered (10PP vaccine or Synflorix™). Vaccine Efficacy (VE) was calculated as 1 minus Relative Risk (i.e. investigational vaccine over control vaccine))

*100].

Comparison groups	10PP-HD 2+1d Group v Synflorix 2+1d Group
Number of subjects included in analysis	394
Analysis specification	Pre-specified
Analysis type	equivalence
Parameter estimate	VE
Point estimate	6.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-18
upper limit	25.7

Statistical analysis title	VE-10PP-HD 2+1d vs Synflorix 2+1d- 3M post-Dose3
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Statistical analysis description:

The analysis aimed to compare occurrences in terms of percentage of subjects with positive nasopharyngeal sample out of the number of subjects with swabs cultured, between 2 groups, three months (M) post-dose 3 of pneumococcal vaccine administered (10PP vaccine or Synflorix™). Vaccine Efficacy (VE) was calculated as 1 minus Relative Risk (i.e. investigational vaccine over control vaccine))*100].

Comparison groups	10PP-HD 2+1d Group v Synflorix 2+1d Group
Number of subjects included in analysis	394
Analysis specification	Pre-specified
Analysis type	equivalence
Parameter estimate	VE
Point estimate	-3.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-29.3
upper limit	17.2

Secondary: Number of subjects with haematological or biochemical abnormalities with respect to normal laboratory ranges – For Cohort 1/Step 1 subjects

End point title	Number of subjects with haematological or biochemical abnormalities with respect to normal laboratory ranges – For Cohort 1/Step 1 subjects ^[11]
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End point description:

Assessed biochemical and haematological parameters were: Haemoglobin (Hgb), White cell count (WBC), Platelet counts, Alanine aminotransferase (ALT) and Creatinine (CREA). Per parameter, it was assessed whether subjects had laboratory values below normal, normal, or above normal range. Below = value below the laboratory reference range defined for the specified time point and laboratory parameter. Within = value within the laboratory reference range defined for the specified time point and laboratory parameter. Above = value above the laboratory reference range defined for the specified time point and laboratory parameter. Unknown = value unknown for the specified time point and laboratory parameter. This outcome concerns subjects enrolled in Cohort 1/Step 1.

End point type	Secondary
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End point timeframe:

At Month 1, or 1 month post vaccination with pneumococcal vaccine (10PP vaccine or Prevnar 13™)

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-HD 1d Group	Prevnar13 1d Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	60		
Units: Subjects				
ALT – Status: Unknown	0	0		
ALT – Status: Below	0	0		
ALT – Status: Within	60	57		
ALT – Status: Above	0	3		
CREA – Status: Unknown	0	0		
CREA – Status: Below	0	0		
CREA – Status: Within	60	60		
CREA – Status: Above	0	0		
Hgb – Status: Unknown	0	0		
Hgb – Status: Below	2	2		
Hgb – Status: Within	57	56		
Hgb – Status: Above	1	2		
Platelets – Status: Unknown	0	0		
Platelets – Status: Below	0	0		
Platelets – Status: Within	59	60		
Platelets – Status: Above	1	0		
WBC – Status: Unknown	0	0		
WBC – Status: Below	0	0		
WBC – Status: Within	60	60		
WBC – Status: Above	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with serious adverse events (SAEs) – For Step 1/Cohort 1 subjects

End point title	Number of subjects with serious adverse events (SAEs) – For Step 1/Cohort 1 subjects ^[12]
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End point description:

SAEs assessed include medical occurrences that result in death, are life threatening, require hospitalization or prolongation of hospitalization, result in disability/incapacity. These should also be considered serious: invasive or malignant cancers, intensive treatment in an emergency room or at home for allergic bronchospasm, blood dyscrasias or convulsions that do not result in hospitalisation. Any = Occurrence of an SAE, regardless of relationship to vaccination. This outcome concerns subjects enrolled in Cohort 1/Step 1.

End point type	Secondary
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End point timeframe:

From Day 0 to Month 6

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-HD 1d Group	Pprevnar13 1d Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	60		
Units: Subjects				
Any SAE(s)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations against pneumococcal pneumolysin toxoid (Ply) and pneumococcal histidine triad protein D (PhtD) proteins – For Cohort 1/Step 1 subjects

End point title	Antibody concentrations against pneumococcal pneumolysin toxoid (Ply) and pneumococcal histidine triad protein D (PhtD) proteins – For Cohort 1/Step 1 subjects ^[13]
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End point description:

Anti-Ply and anti-PhtD antibody concentrations were measured by Multiplex immunoassay and expressed as geometric mean concentrations (GMCs), in Luminex Units per milliliter (LU/mL). Cut-off of the assay were concentrations higher than or equal to (\geq) 599 LU/mL for anti-Ply antibodies and \geq 391 LU/mL for anti-PhtD antibodies. This outcome concerns subjects enrolled in Cohort 1/Step 1.

End point type	Secondary
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End point timeframe:

At Month 1, or 1 month post vaccination with pneumococcal vaccine (10PP vaccine or Pprevnar 13™)

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-HD 1d Group	Pprevnar13 1d Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	51		
Units: LU/mL				
geometric mean (confidence interval 95%)				
Anti-Ply	22794.9 (17570.1 to 29573.3)	8510.3 (6668.5 to 10860.8)		
Anti-PhtD	31326.3 (26293.9 to 37321.8)	16810 (13516.3 to 20906.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations against Protein D (PD) – For Cohort 1/Step 1 subjects

End point title	Antibody concentrations against Protein D (PD) – For Cohort 1/Step 1 subjects ^[14]
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End point description:

Anti-PD antibody concentrations were measured by Multiplex immunoassay, expressed as geometric mean concentrations (GMCs), in Luminex Units per milliliter (LU/mL). The cut-off of the assay was an anti-PD antibody concentration higher than or equal to (\geq) 112 LU/mL. This outcome concerns subjects enrolled in Cohort 1/Step 1.

End point type	Secondary
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End point timeframe:

At Month 1, or 1 month post vaccination with pneumococcal vaccine (10PP vaccine or Prevnar 13™)

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-HD 1d Group	Prevnar13 1d Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	51		
Units: LU/mL				
geometric mean (confidence interval 95%)				
Anti-PD	137.5 (108.4 to 174.4)	65.1 (58.2 to 72.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations against vaccine serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F – For Cohort 1/Step 1 subjects

End point title	Antibody concentrations against vaccine serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F – For Cohort 1/Step 1 subjects ^[15]
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End point description:

Antibody concentrations were measured by 22F-inhibition Enzyme-Linked ImmunoSorbent Assay (ELISA), expressed as geometric mean concentrations (GMCs), in micrograms per milliliter ($\mu\text{g/mL}$). The cut-off of the assay was an antibody concentration higher than or equal to (\geq) 0.05 $\mu\text{g/mL}$. This outcome concerns subjects enrolled in Cohort 1/Step 1.

End point type	Secondary
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End point timeframe:

At Month 1, or 1 month post vaccination with pneumococcal vaccine (10PP vaccine or Pevnar 13™)

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-HD 1d Group	Pevnar13 1d Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	51		
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-1 antibodies	1.71 (1.33 to 2.22)	3.12 (2.44 to 4.01)		
Anti-4 antibodies	4.8 (3.75 to 6.14)	4.17 (3.33 to 5.21)		
Anti-5 antibodies	1.17 (0.88 to 1.55)	1.47 (1.08 to 1.99)		
Anti-6B antibodies	0.5 (0.34 to 0.73)	1.57 (0.98 to 2.51)		
Anti-7F antibodies	2.44 (1.99 to 2.98)	6.11 (4.44 to 8.41)		
Anti-9V antibodies	0.89 (0.71 to 1.12)	2.41 (1.87 to 3.26)		
Anti-14 antibodies	1.88 (1.39 to 2.53)	3.77 (2.61 to 5.43)		
Anti-18C antibodies	7.58 (5.43 to 10.57)	4.82 (3.46 to 6.71)		
Anti-19F antibodies	7.82 (5.84 to 10.46)	5.95 (4.48 to 7.9)		
Anti-23F antibodies	0.31 (0.21 to 0.46)	1.11 (0.74 to 1.67)		

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations against vaccine serotypes 3, 6A and 19A – For Cohort 1/Step 1 subjects

End point title	Antibody concentrations against vaccine serotypes 3, 6A and 19A – For Cohort 1/Step 1 subjects ^[16]
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End point description:

Antibody concentrations were measured by 22F-inhibition Enzyme-Linked ImmunoSorbent Assay (ELISA), expressed as geometric mean concentrations (GMCs), in micrograms per milliliter (µg/mL). The cut-off of the assay was an antibody concentration higher than or equal to (\geq) 0.05 µg/mL. This outcome concerns subjects enrolled in Cohort 1/Step 1.

End point type	Secondary
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End point timeframe:

At Month 1, or 1 month post vaccination with pneumococcal vaccine (10PP vaccine or Pevnar 13™)

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-HD 1d Group	Pprevnar13 1d Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	51		
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-3 antibodies	0.25 (0.14 to 0.46)	2.35 (1.77 to 3.12)		
Anti-6A antibodies	0.18 (0.12 to 0.27)	1.36 (0.96 to 1.93)		
Anti-19A antibodies	1.38 (0.91 to 2.1)	5.51 (4.02 to 7.55)		

Statistical analyses

No statistical analyses for this end point

Secondary: Titers for opsonophagocytic activity against vaccine serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F – For Cohort 1/Step 1 subjects

End point title	Titers for opsonophagocytic activity against vaccine serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F – For Cohort 1/Step 1 subjects ^[17]
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End point description:

The cut-off of the assay was a titer for opsonophagocytic activity higher than or equal to (\geq) 8. This outcome concerns subjects enrolled in Cohort 1/Step 1.

End point type	Secondary
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End point timeframe:

At Month 1, or 1 month post vaccination with pneumococcal vaccine (10PP vaccine or Pprevnar 13™)

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-HD 1d Group	Pprevnar13 1d Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	51		
Units: Titers				
geometric mean (confidence interval 95%)				
OPSONO-1 (N=52;50)	17.2 (11.2 to 26.4)	112.8 (71.9 to 177)		

OPSONO-4 (N=52;51)	2818.9 (2009.7 to 3953.8)	4162.3 (3123.9 to 5545.9)		
OPSONO-5 (N=52;49)	9 (6.4 to 12.7)	89.8 (55.8 to 144.5)		
OPSONO-6B (N=50;51)	345.3 (171.4 to 695.5)	5082.5 (3700.2 to 6981.2)		
OPSONO-7F (N=52;51)	6214 (5217.1 to 7401.4)	17781 (14034.2 to 22528)		
OPSONO-9V (N=52;51)	2880.8 (2264.8 to 3664.5)	12687.8 (9188.2 to 17520.2)		
OPSONO-14 (N=51;51)	1116.1 (715.5 to 1741)	5985.9 (4313.1 to 8307.4)		
OPSONO-18C (N=52;49)	3955.4 (3027.7 to 5167.2)	2799.8 (1931.1 to 4059.2)		
OPSONO-19F (N=52;51)	862.9 (529.2 to 1407)	452.8 (276.2 to 742.2)		
OPSONO-23F (N=51;51)	2756.7 (1638 to 4639.5)	12652.4 (8076 to 19822.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Titers for opsonophagocytic activity against vaccine serotypes 3, 6A and 19A – For Cohort 1/Step 1 subjects

End point title	Titers for opsonophagocytic activity against vaccine serotypes 3, 6A and 19A – For Cohort 1/Step 1 subjects ^[18]
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End point description:

The cut-off of the assay was a titer for opsonophagocytic activity higher than or equal to (\geq) 8. This outcome concerns subjects enrolled in Cohort 1/Step 1.

End point type	Secondary
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End point timeframe:

At Month 1, or 1 month post vaccination with pneumococcal vaccine (10PP vaccine or Prevnar 13™)

Notes:

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-HD 1d Group	Prevnar13 1d Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	51	51		
Units: Titers				
geometric mean (confidence interval 95%)				
OPSONO-3 (N=51;51)	10.1 (6.5 to 15.8)	152.5 (120.4 to 193.2)		

OPSONO-6A (N=47;51)	212.7 (110.4 to 410)	8488.8 (5984.2 to 12041.8)		
OPSONO-19A (N=49;50)	461.7 (277.2 to 769)	970.3 (701 to 1342.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of antibodies inhibiting pneumococcal pneumolysin toxoid (Ply) haemolysis activity, or Hem-Ply antibodies – For Cohort 1/Step 1 subjects

End point title	Concentrations of antibodies inhibiting pneumococcal pneumolysin toxoid (Ply) haemolysis activity, or Hem-Ply antibodies – For Cohort 1/Step 1 subjects ^[19]
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End point description:

Concentrations of Hem-Ply antibodies were expressed as geometric mean titers . The cut-off of the assay was an Hem-Ply antibody titer ≥ 140 . This outcome concerns subjects enrolled in Cohort 1/Step 1.

End point type	Secondary
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End point timeframe:

At Month 1, or 1 month post vaccination with pneumococcal vaccine (10PP vaccine or Prevnar 13™)

Notes:

[19] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-HD 1d Group	Prevnar13 1d Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	51		
Units: Titers				
geometric mean (confidence interval 95%)				
Hem-Ply antibodies	682.3 (562.8 to 827.3)	534 (439.4 to 648.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any and Grade 3 solicited local symptoms – For Cohort2/Step 2 subjects receiving the 3+0 Schedule

End point title	Number of subjects with any and Grade 3 solicited local symptoms – For Cohort2/Step 2 subjects receiving the 3+0 Schedule ^[20]
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End point description:

Assessed local symptoms were pain, redness and swelling. Any = Occurrence of the specified solicited local symptom, regardless of intensity. Grade 3 Pain = Crying when limb was moved/spontaneously

painful. Grade 3 Redness/Swelling = Redness/swelling at injection site larger than (>) 30 millimeters (mm). This outcome concerns Cohort2/Step 2 subjects receiving the 3+0 Schedule.

End point type	Secondary
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End point timeframe:

Within the 4-day (Days 0-3) periods post vaccination with 3 doses of pneumococcal vaccine (10PP vaccine, Synflorix™ or Prevnar 13™), across doses

Notes:

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-LD 3+0d Group	10PP-HD 3+0d Group	Synflorix 3+0d Group	Prevnar13 3+0d Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	200	200	200	200
Units: Subjects				
Any pain	108	121	123	115
Grade 3 pain	0	1	0	0
Any redness	8	7	9	5
Grade 3 redness	0	1	1	0
Any swelling	30	45	40	37
Grade 3 swelling	7	10	17	7

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any and Grade 3 solicited local symptoms – For Cohort2/Step 2 subjects receiving the 2+1 Schedule

End point title	Number of subjects with any and Grade 3 solicited local symptoms – For Cohort2/Step 2 subjects receiving the 2+1 Schedule ^[21]
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End point description:

Assessed local symptoms were pain, redness and swelling. Any = Occurrence of the specified solicited local symptom, regardless of intensity. Grade 3 Pain = Crying when limb was moved/spontaneously painful. Grade 3 Redness/Swelling = Redness/swelling at injection site larger than (>) 30 millimeters (mm). This outcome concerns Cohort2/Step 2 subjects receiving the 2+1 Schedule.

End point type	Secondary
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End point timeframe:

Within the 4-day (Days 0-3) periods post vaccination with the 2 first doses of pneumococcal vaccine (10PP vaccine or Synflorix™), across doses

Notes:

[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-HD 2+1d Group	Synflorix 2+1d Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	200	200		
Units: Subjects				
Any pain	97	102		
Grade 3 pain	1	1		
Any redness	3	5		
Grade 3 redness	0	0		
Any swelling	35	31		
Grade 3 swelling	9	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any and Grade 3 solicited local symptoms – For Cohort2/Step 2 subjects receiving the 2+1 Schedule

End point title	Number of subjects with any and Grade 3 solicited local symptoms – For Cohort2/Step 2 subjects receiving the 2+1 Schedule ^[22]
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End point description:

Assessed local symptoms were pain, redness and swelling. Any = Occurrence of the specified solicited local symptom, regardless of intensity. Grade 3 Pain = Crying when limb was moved/spontaneously painful. Grade 3 Redness/Swelling = Redness/swelling at injection site larger than (>) 30 millimeters (mm). This outcome concerns Cohort2/Step 2 subjects receiving the 2+1 Schedule.

End point type	Secondary
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End point timeframe:

Within the 4-day (Days 0-3) period post vaccination with Dose 3 of pneumococcal vaccine (10PP vaccine or Synflorix™)

Notes:

[22] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-HD 2+1d Group	Synflorix 2+1d Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	191	195		
Units: Subjects				
Any pain	21	26		
Grade 3 pain	0	0		
Any redness	0	0		
Grade 3 redness	0	0		
Any swelling	4	8		
Grade 3 swelling	1	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any and Grade 3 solicited general symptoms and with solicited general symptoms with relationship to vaccination – For Step 2/Cohort 2 subjects receiving the 3+0 Schedule

End point title	Number of subjects with any and Grade 3 solicited general symptoms and with solicited general symptoms with relationship to vaccination – For Step 2/Cohort 2 subjects receiving the 3+0 Schedule ^[23]
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End point description:

Assessed solicited general symptoms were Drowsiness, Fever (axillary temperature higher than [\geq] 37.5 degrees Celsius [$^{\circ}$ C]), Irritability/Fussiness and Loss of appetite. Any = Occurrence of the specified solicited general symptom, regardless of intensity. Related = Occurrence of the specified symptom assessed by the investigators as causally related to vaccination. Grade 3 Drowsiness = Drowsiness that prevented normal activity. Grade 3 Fever = Axillary temperature higher than ($>$) 39.5 $^{\circ}$ C. Grade 3 Irritability/fussiness = Crying that could not be comforted/prevented normal activity. Grade 3 Loss of appetite = Subject did not eat at all. This outcome concerns Step 2/Cohort 2 subjects receiving the 3+0 Schedule.

End point type	Secondary
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End point timeframe:

Within the 4-day (Days 0-3) periods post vaccination with 3 doses of pneumococcal vaccine (10PP vaccine, Synflorix[™] or Prevnar 13[™]), across doses

Notes:

[23] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-LD 3+0d Group	10PP-HD 3+0d Group	Synflorix 3+0d Group	Prevnar13 3+0d Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	200	200	200	200
Units: Subjects				
Any Drowsiness	43	46	38	44
Grade 3 Drowsiness	0	0	0	0
Related Drowsiness	43	45	38	43
Any Irritability/fussiness	139	133	141	136
Grade 3 Irritability/fussiness	6	4	4	7
Related Irritability/fussiness	138	132	138	136
Any Loss of appetite	32	30	27	34
Grade 3 Loss of appetite	0	0	1	0
Related Loss of appetite	32	29	26	34
Any Fever	104	100	105	106
Grade 3 Fever	0	0	0	0
Related Fever	102	100	104	104

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any and Grade 3 solicited general symptoms and with solicited general symptoms with relationship to vaccination – For Step 2/Cohort 2 subjects receiving the 2+1 Schedule

End point title	Number of subjects with any and Grade 3 solicited general symptoms and with solicited general symptoms with relationship to vaccination – For Step 2/Cohort 2 subjects receiving the 2+1 Schedule ^[24]
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End point description:

Assessed solicited general symptoms were Drowsiness, Fever (axillary temperature higher than [\geq] 37.5 degrees Celsius [$^{\circ}\text{C}$]), Irritability/Fussiness and Loss of appetite. Any = Occurrence of the specified solicited general symptom, regardless of intensity. Related = Occurrence of the specified symptom assessed by the investigators as causally related to vaccination. Grade 3 Drowsiness = Drowsiness that prevented normal activity. Grade 3 Fever = Axillary temperature higher than ($>$) 39.5 $^{\circ}\text{C}$. Grade 3 Irritability/fussiness = Crying that could not be comforted/prevented normal activity. Grade 3 Loss of appetite = Subject did not eat at all. This outcome concerns Step 2/Cohort 2 subjects receiving the 2+1 Schedule.

End point type	Secondary
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End point timeframe:

Within the 4-day (Days 0-3) periods post vaccination with the 2 first doses of pneumococcal vaccine (10PP vaccine or SynflorixTM), across doses

Notes:

[24] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-HD 2+1d Group	Synflorix 2+1d Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	200	200		
Units: Subjects				
Any Drowsiness	47	44		
Grade 3 Drowsiness	0	0		
Related Drowsiness	46	43		
Any Fever	92	84		
Grade 3 Fever	0	0		
Related Fever	89	84		
Any Irritability/fussiness	131	128		
Grade 3 Irritability/fussiness	1	2		
Related Irritability/fussiness	128	126		
Any Loss of appetite	24	25		
Grade 3 Loss of appetite	0	0		
Related Loss of appetite	24	24		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any and Grade 3 solicited general symptoms and with solicited general symptoms with relationship to vaccination – For Step 2/Cohort 2 subjects receiving the 2+1 Schedule

End point title	Number of subjects with any and Grade 3 solicited general symptoms and with solicited general symptoms with
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End point description:

Assessed solicited general symptoms were Drowsiness, Fever (axillary temperature higher than \geq 37.5 degrees Celsius [$^{\circ}$ C]), Irritability/Fussiness and Loss of appetite. Any = Occurrence of the specified solicited general symptom, regardless of intensity. Related = Occurrence of the specified symptom assessed by the investigators as causally related to vaccination. Grade 3 Drowsiness = Drowsiness that prevented normal activity. Grade 3 Fever = Axillary temperature higher than ($>$) 39.5 $^{\circ}$ C. Grade 3 Irritability/fussiness = Crying that could not be comforted/prevented normal activity. Grade 3 Loss of appetite = Subject did not eat at all. This outcome concerns Step 2/Cohort 2 subjects receiving the 2+1 Schedule.

End point type	Secondary
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End point timeframe:

Within the 4-day (Days 0-3) period post vaccination with Dose 3 of pneumococcal vaccine (10PP vaccine or SynflorixTM)

Notes:

[25] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-HD 2+1d Group	Synflorix 2+1d Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	191	195		
Units: Subjects				
Any Drowsiness	12	4		
Grade 3 Drowsiness	0	0		
Related Drowsiness	12	4		
Any Fever	32	27		
Grade 3 Fever	0	1		
Related Fever	30	25		
Any Irritability/fussiness	27	19		
Grade 3 Irritability/fussiness	0	0		
Related Irritability/fussiness	27	19		
Any Loss of appetite	3	5		
Grade 3 Loss of appetite	0	0		
Related Loss of appetite	3	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any unsolicited adverse events (AEs) – For Step 2/Cohort 2 subjects receiving the 3+0 Schedule

End point title	Number of subjects with any unsolicited adverse events (AEs) – For Step 2/Cohort 2 subjects receiving the 3+0 Schedule ^[26]
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End point description:

An unsolicited 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. An AE can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a medicinal product. For marketed medicinal products, this also includes failure to produce expected

benefits (i.e. lack of efficacy), abuse or misuse. Any = Occurrence of an unsolicited AE, regardless of intensity or relationship to vaccination. This outcome concerns Step 2/Cohort 2 subjects receiving the 3+0 Schedule.

End point type	Secondary
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End point timeframe:

Within the 31-day (Days 0-30) periods post vaccination with 3 doses of pneumococcal vaccine (10PP vaccine, Synflorix™ or Prevnar 13™), across doses

Notes:

[26] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-LD 3+0d Group	10PP-HD 3+0d Group	Synflorix 3+0d Group	Prevnar13 3+0d Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	200	200	200	200
Units: Subjects				
Any AE(s)	113	114	123	114

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any unsolicited adverse events (AEs) – For Step 2/Cohort 2 subjects receiving the 2+1 Schedule

End point title	Number of subjects with any unsolicited adverse events (AEs) – For Step 2/Cohort 2 subjects receiving the 2+1 Schedule ^[27]
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End point description:

An unsolicited 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. An AE can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a medicinal product. For marketed medicinal products, this also includes failure to produce expected benefits (i.e. lack of efficacy), abuse or misuse. Any = Occurrence of an unsolicited AE, regardless of intensity or relationship to vaccination. This outcome concerns Step 2/Cohort 2 subjects receiving the 2+1 Schedule.

End point type	Secondary
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End point timeframe:

Within the 31-day (Days 0-30) periods post vaccination with the 2 first doses of pneumococcal vaccine (10PP vaccine or Synflorix™), across doses

Notes:

[27] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-HD 2+1d Group	Synflorix 2+1d Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	200	200		
Units: Subjects				
Any AE(s)	84	95		

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations against pneumococcal pneumolysin toxoid (Ply) and pneumococcal histidine triad protein D (PhtD) proteins – For Cohort 2/Step 2 subjects receiving the 3+0 Schedule

End point title	Antibody concentrations against pneumococcal pneumolysin toxoid (Ply) and pneumococcal histidine triad protein D (PhtD) proteins – For Cohort 2/Step 2 subjects receiving the 3+0 Schedule ^[28]
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End point description:

Anti-Ply and anti-PhtD antibody concentrations were measured by Enzyme-linked immunosorbent assay (ELISA) immunoassay and expressed as geometric mean concentrations (GMCs), in ELISA Units per milliliter (EL.U/mL).

Cut-off of the assay were concentrations higher than or equal to (\geq) 12 EL.U/mL for anti-Ply antibodies and \geq 17 EL.U/mL for anti-PhtD antibodies. This outcome concerns subjects enrolled in Cohort 2/Step 2 who received the 3+0 Schedule.

End point type	Secondary
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End point timeframe:

At 1, 5 and 8 months (Mth) post-Dose 3 of pneumococcal vaccine administered (10PP vaccine, Synflorix[™] or Prevnar 13[™])

Notes:

[28] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-LD 3+0d Group	10PP-HD 3+0d Group	Synflorix 3+0d Group	Prevnar13 3+0d Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	192	195	196	195
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-Ply 1 Mth post dose 3 (N=192, 195, 196, 195)	13968.86 (12612.27 to 15471.36)	16771.16 (15267.84 to 18422.51)	451.32 (398.68 to 510.91)	419.47 (377.26 to 466.4)
Anti-Ply 5 Mth post dose 3 (N=191, 192, 195, 190)	11268.35 (9870.36 to 12864.36)	10817.78 (9528.87 to 12281.04)	744.86 (631.27 to 878.89)	637.49 (539.55 to 753.22)
Anti-Ply 8 Mth post dose 3 (N=189, 190, 195, 188)	10512.39 (9249.03 to 11948.33)	10299.57 (9137.48 to 11609.44)	999.39 (861.41 to 1159.49)	884.83 (748.83 to 1045.54)
Anti-PhtD 1 Mth post dose 3 (N=192, 195, 196, 195)	2584.28 (2292.67 to 2912.98)	2188.28 (1934.94 to 2474.8)	334.18 (292.9 to 381.28)	486.01 (419.64 to 562.87)

Anti-PhtD 5 Mth post dose 3 (N=191, 192, 195, 190)	2242.06 (1971.08 to 2550.29)	1498.86 (1311.05 to 1713.57)	936.83 (780.23 to 1124.86)	1419.77 (1196.01 to 1685.4)
Anti-PhtD 8 Mth post dose 3 (N=189, 190, 195, 188)	2608.78 (2318.09 to 2935.92)	2078.35 (1861.91 to 2319.95)	1667.91 (1432.09 to 1942.55)	2380.09 (2118.18 to 2674.39)

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations against pneumococcal pneumolysin toxoid (Ply) and pneumococcal histidine triad protein D (PhtD) proteins – For Cohort 2/Step 2 subjects receiving the 2+1 Schedule

End point title	Antibody concentrations against pneumococcal pneumolysin toxoid (Ply) and pneumococcal histidine triad protein D (PhtD) proteins – For Cohort 2/Step 2 subjects receiving the 2+1 Schedule ^[29]
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End point description:

Anti-Ply and anti-PhtD antibody concentrations were measured by Enzyme-linked immunosorbent assay (ELISA) immunoassay and expressed as geometric mean concentrations (GMCs), in ELISA Units per milliliter (EL.U/mL).

Cut-off of the assay were concentrations higher than or equal to (\geq) 12 EL.U/mL for anti-Ply antibodies and \geq 17 EL.U/mL for anti-PhtD antibodies. This outcome concerns subjects enrolled in Cohort 2/Step 2 who received the 2+1 Schedule.

End point type	Secondary
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End point timeframe:

At 1 and 5 months (Mth) post-Dose 2, and at 3 months post-Dose 3 of the pneumococcal vaccine administered (10PP vaccine or Synflorix™)

Notes:

[29] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-HD 2+1d Group	Synflorix 2+1d Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	193	193		
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-Ply 1 Mth post dose 2 (N=193, 193)	11491.54 (10168.1 to 12987.23)	488.79 (427.38 to 559.01)		
Anti-Ply 5 Mth post dose 2 (N=189, 191)	7453.65 (6460.7 to 8599.21)	807.67 (676.2 to 964.7)		
Anti-Ply 3 Mth post dose 3 (N=190, 190)	17933.07 (15867 to 20268.17)	1114.25 (945.08 to 1313.71)		
Anti-PhtD 1 Mth post dose 2 (N=193, 193)	1264.57 (1103.87 to 1448.66)	368.62 (319.88 to 424.79)		

Anti-PhtD 5 Mth post dose 2 (N=189, 191)	1448.08 (1253.08 to 1673.41)	1036.53 (853.8 to 1258.36)		
Anti-PhtD 3 Mth post dose 3 (N=190, 190)	3250.91 (2956.18 to 3575.02)	1654.79 (1415.54 to 1934.47)		

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations against Protein D (PD) – For Cohort 2/Step 2 subjects receiving the 3+0 Schedule

End point title	Antibody concentrations against Protein D (PD) – For Cohort 2/Step 2 subjects receiving the 3+0 Schedule ^[30]
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End point description:

Anti-PD antibody concentrations were measured by Enzyme-linked immunosorbent assay (ELISA) immunoassay, expressed as geometric mean concentrations (GMCs), in ELISA Units per milliliter (EL.U/mL). The cut-off of the assay was anti-PD antibody concentration higher than or equal to (\geq) 100 EL.U/mL. This outcome concerns subjects enrolled in Cohort 2/Step 2 who received the 3+0 Schedule.

End point type	Secondary
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End point timeframe:

At 1, 5 and 8 months (Mth) post-Dose 3 of pneumococcal vaccine administered (10PP vaccine, Synflorix™ or Prevnar 13™)

Notes:

[30] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-LD 3+0d Group	10PP-HD 3+0d Group	Synflorix 3+0d Group	Prevnar13 3+0d Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	191	193	194	189
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PD 1 Mth post dose 3 (N=186, 193, 187, 189)	1922.8 (1739.3 to 2125.6)	1833.8 (1628.5 to 2065)	1990.2 (1765.7 to 2243.3)	84.8 (76.4 to 94.1)
Anti-PD 5 Mth post dose 3 (N=191, 191, 193, 185)	559.2 (496.8 to 629.6)	499.2 (439.9 to 566.5)	609.9 (537 to 692.8)	83.1 (74.9 to 92.2)
Anti-PD 8 Mth post dose 3 (N=187, 190, 194, 187)	324.3 (282.2 to 372.7)	288.2 (248.5 to 334.2)	344.2 (300.6 to 394.2)	69.2 (63.6 to 75.3)

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations against Protein D (PD) – For Cohort 2/Step 2 subjects receiving the 2+1 Schedule

End point title	Antibody concentrations against Protein D (PD) – For Cohort 2/Step 2 subjects receiving the 2+1 Schedule ^[31]
End point description: Anti-PD antibody concentrations were measured by Enzyme-linked immunosorbent assay (ELISA) immunoassay, expressed as geometric mean concentrations (GMCs), in ELISA Units per milliliter (EL.U/mL). The cut-off of the assay was anti-PD antibody concentration higher than or equal to (\geq) 100 EL.U/mL. This outcome concerns subjects enrolled in Cohort 2/Step 2 who received the 2+1 Schedule.	
End point type	Secondary
End point timeframe: At 1 and 5 months (Mth) post-Dose 2, and at 3 months post-Dose 3 of the pneumococcal vaccine administered (10PP vaccine or Synflorix™)	

Notes:

[31] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-HD 2+1d Group	Synflorix 2+1d Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	190	190		
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PD 1 Mth post dose 2 (N=187, 187)	990.9 (869.3 to 1129.5)	1126.7 (999.4 to 1270.2)		
Anti-PD 5 Mth post dose 2 (N=188, 187)	281.3 (247.5 to 319.7)	313 (276.2 to 354.7)		
Anti-PD 3 Mth post dose 3 (N=190, 190)	534.8 (468.9 to 610)	664.9 (580.1 to 762.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations against vaccine serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F – For Cohort 2/Step 2 subjects who received the 3+0 Schedule

End point title	Antibody concentrations against vaccine serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F – For Cohort 2/Step 2 subjects who received the 3+0 Schedule ^[32]
End point description: Antibody concentrations were measured by 22F-inhibition Enzyme-Linked ImmunoSorbent Assay (ELISA), expressed as geometric mean concentrations (GMCs), in micrograms per milliliter (µg/mL). The cut-off of the assay was an antibody concentration higher than or equal to (\geq) 0.05 µg/mL. This outcome concerns subjects enrolled in Cohort 2/Step 2 who received the 3+0 Schedule.	
End point type	Secondary
End point timeframe: At 1, 5 and 8 months (Mth) post-Dose 3 of pneumococcal vaccine administered (10PP vaccine, Synflorix™ or Prevnar 13™)	

Notes:

[32] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned

End point values	10PP-LD 3+0d Group	10PP-HD 3+0d Group	Synflorix 3+0d Group	Prevnar13 3+0d Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	191	195	196	195
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-1 1 Mth post dose 3 (N=191, 194, 193, 193)	3.58 (3.17 to 4.03)	3.2 (2.82 to 3.63)	3.38 (2.98 to 3.83)	5.51 (4.92 to 6.17)
Anti-1 5 Mth post dose 3 (N=190, 192, 195, 189)	0.67 (0.59 to 0.76)	0.55 (0.49 to 0.63)	0.62 (0.55 to 0.71)	1.16 (1.05 to 1.29)
Anti-1 8 Mth post dose 3 (N=189, 189, 194, 187)	0.4 (0.35 to 0.45)	0.35 (0.31 to 0.4)	0.4 (0.35 to 0.46)	0.83 (0.73 to 0.93)
Anti-4 1 Mth post dose 3 (N=191, 195, 195, 192)	3.89 (3.43 to 4.41)	3.15 (2.75 to 3.6)	3.75 (3.29 to 4.28)	6.25 (5.63 to 6.93)
Anti-4 5 Mth post dose 3 (N=191, 192, 194, 190)	1.19 (1.06 to 1.34)	1.04 (0.93 to 1.16)	1.14 (1 to 1.29)	1.06 (0.94 to 1.19)
Anti-4 8 Mth post dose 3 (N=189, 190, 195, 188)	0.7 (0.62 to 0.79)	0.59 (0.52 to 0.68)	0.66 (0.58 to 0.76)	0.54 (0.48 to 0.61)
Anti-5 1 Mth post dose 3 (N=186, 193, 187, 190)	5.17 (4.54 to 5.88)	4.83 (4.21 to 5.54)	5.3 (4.66 to 6.02)	7.02 (6.14 to 8.02)
Anti-5 5 Mth post dose 3 (N=190, 192, 194, 190)	1.37 (1.21 to 1.55)	1.25 (1.1 to 1.43)	1.33 (1.17 to 1.51)	1.79 (1.59 to 2.02)
Anti-5 8 Mth post dose 3 (N=189, 187, 194, 187)	0.73 (0.65 to 0.83)	0.68 (0.59 to 0.79)	0.69 (0.6 to 0.79)	1.12 (0.99 to 1.27)
Anti-6B 1 Mth post dose 3 (N=190, 194, 192, 191)	0.91 (0.74 to 1.12)	0.69 (0.56 to 0.86)	1 (0.8 to 1.25)	1.35 (1.11 to 1.65)
Anti-6B 5 Mth post dose 3 (N=190, 190, 194, 189)	1.1 (0.94 to 1.29)	0.86 (0.73 to 1.01)	1.24 (1.06 to 1.44)	0.38 (0.33 to 0.44)
Anti-6B 8 Mth post dose 3 (N=189, 189, 195, 188)	0.87 (0.75 to 1)	0.73 (0.62 to 0.86)	0.96 (0.83 to 1.11)	0.29 (0.26 to 0.34)
Anti-7F 1 Mth post dose 3 (N=190, 194, 195, 195)	4.63 (4.1 to 5.22)	4.1 (3.62 to 4.63)	4.29 (3.77 to 4.88)	5.53 (4.96 to 6.17)
Anti-7F 5 Mth post dose 3 (N=191, 192, 195, 190)	2.24 (2.01 to 2.5)	1.84 (1.63 to 2.08)	2.19 (1.95 to 2.47)	2.21 (1.99 to 2.45)
Anti-7F 8 Mth post dose 3 (N=189, 190, 195, 188)	1.54 (1.38 to 1.72)	1.31 (1.15 to 1.5)	1.57 (1.39 to 1.78)	1.65 (1.49 to 1.82)
Anti-9V 1 Mth post dose 3 (N=188, 194, 196, 194)	3.23 (2.83 to 3.68)	3.25 (2.83 to 3.72)	3.26 (2.82 to 3.78)	4.02 (3.45 to 4.69)
Anti-9V 5 Mth post dose 3 (N=191, 192, 193, 189)	1.35 (1.2 to 1.53)	1.15 (1.02 to 1.3)	1.33 (1.17 to 1.52)	0.83 (0.72 to 0.95)
Anti-9V 8 Mth post dose 3 (N=189, 189, 195, 188)	1.09 (0.95 to 1.25)	0.87 (0.77 to 1)	1.08 (0.95 to 1.23)	0.63 (0.55 to 0.73)
Anti-14 1 Mth post dose 3 (N=191, 193, 192, 194)	4.36 (3.7 to 5.13)	4.11 (3.49 to 4.85)	4.15 (3.52 to 4.89)	4.66 (3.93 to 5.52)
Anti-14 5 Mth post dose 3 (N=190, 192, 194, 189)	2.15 (1.84 to 2.5)	1.86 (1.56 to 2.22)	2.13 (1.77 to 2.56)	3.43 (2.89 to 4.06)
Anti-14 8 Mth post dose 3 (N=189, 190, 195, 188)	1.38 (1.18 to 1.61)	1.37 (1.15 to 1.63)	1.42 (1.18 to 1.71)	2.47 (2.1 to 2.92)
Anti-18C 1 Mth post dose 3 (N=186, 194, 189, 193)	15.88 (13.8 to 18.26)	14.84 (12.88 to 17.09)	15.66 (13.52 to 18.14)	5.78 (5.03 to 6.64)
Anti-18C 5 Mth post dose 3 (N=191, 192, 195, 190)	4.09 (3.54 to 4.71)	3.52 (3.06 to 4.05)	4.17 (3.6 to 4.83)	0.95 (0.84 to 1.06)
Anti-18C 8 Mth post dose 3 (N=189, 190, 195, 188)	2.18 (1.9 to 2.51)	1.82 (1.58 to 2.1)	2.24 (1.95 to 2.58)	0.66 (0.58 to 0.75)
Anti-19F 1 Mth post dose 3 (N=189, 193, 193, 193)	9.47 (8.08 to 11.09)	9.36 (8.04 to 10.91)	10.04 (8.54 to 11.8)	5.99 (5.4 to 6.64)

Anti-19F 5 Mth post dose 3 (N=190, 191, 195, 188)	2.65 (2.29 to 3.07)	2.34 (2.03 to 2.71)	3.11 (2.67 to 3.62)	0.96 (0.83 to 1.11)
Anti-19F 8 Mth post dose 3 (N=189, 188, 194, 187)	1.65 (1.4 to 1.93)	1.45 (1.22 to 1.72)	1.99 (1.68 to 2.35)	0.55 (0.46 to 0.66)
Anti-23F 1 Mth post dose 3 (N=185, 194, 189, 192)	1.18 (0.98 to 1.42)	1.14 (0.95 to 1.38)	1.22 (0.99 to 1.51)	2.92 (2.47 to 3.44)
Anti-23F 5 Mth post dose 3 (N=191, 192, 195, 190)	0.78 (0.66 to 0.93)	0.77 (0.66 to 0.89)	0.9 (0.77 to 1.06)	0.47 (0.4 to 0.57)
Anti-23F 8 Mth post dose 3 (N=189, 190, 195, 188)	0.62 (0.53 to 0.73)	0.59 (0.49 to 0.7)	0.68 (0.58 to 0.79)	0.39 (0.31 to 0.48)

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations against vaccine serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F – For Cohort 2/Step 2 subjects who received the 2+1 Schedule

End point title	Antibody concentrations against vaccine serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F – For Cohort 2/Step 2 subjects who received the 2+1 Schedule ^[33]
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End point description:

Antibody concentrations were measured by 22F-inhibition Enzyme-Linked ImmunoSorbent Assay (ELISA), expressed as geometric mean concentrations (GMCs), in micrograms per milliliter (µg/mL). The cut-off of the assay was an antibody concentration higher than or equal to (\geq) 0.05 µg/mL. This outcome concerns subjects enrolled in Cohort 2/Step 2 who received the 2+1 Schedule.

End point type	Secondary
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End point timeframe:

At 1 and 5 months (Mth) post-Dose 2, and at 3 months post-Dose 3 of the pneumococcal vaccine administered (10PP vaccine or Synflorix™)

Notes:

[33] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-HD 2+1d Group	Synflorix 2+1d Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	193	193		
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-1 1 Mth post dose 2 (N=192, 191)	2.52 (2.22 to 2.86)	2.41 (2.13 to 2.72)		
Anti-1 5 Mth post dose 2 (N=189, 191)	0.44 (0.39 to 0.49)	0.42 (0.37 to 0.48)		
Anti-1 3 Mth post dose 3 (N=190, 190)	1.65 (1.43 to 1.9)	1.61 (1.41 to 1.83)		
Anti-4 1 Mth post dose 2 (N=192, 193)	2.79 (2.42 to 3.22)	2.67 (2.3 to 3.09)		
Anti-4 5 Mth post dose 2 (N=189, 190)	0.79 (0.7 to 0.89)	0.76 (0.67 to 0.86)		
Anti-4 3 Mth post dose 3 (N=190, 190)	2.15 (1.91 to 2.42)	1.92 (1.71 to 2.16)		

Anti-5 1 Mth post dose 2 (N=188, 186)	3.74 (3.29 to 4.26)	3.4 (2.96 to 3.91)		
Anti-5 5 Mth post dose 2 (N=188, 190)	1.07 (0.95 to 1.21)	0.92 (0.81 to 1.04)		
Anti-5 3 Mth post dose 3 (N=190, 190)	2.86 (2.53 to 3.23)	2.34 (2.04 to 2.69)		
Anti-6B 1 Mth post dose 2 (N=189, 189)	0.51 (0.4 to 0.64)	0.51 (0.41 to 0.64)		
Anti-6B 5 Mth post dose 2 (N=186, 189)	0.63 (0.53 to 0.75)	0.67 (0.58 to 0.79)		
Anti-6B 3 Mth post dose 3 (N=190, 190)	1.35 (1.17 to 1.56)	1.39 (1.21 to 1.61)		
Anti-7F 1 Mth post dose 2 (N=192, 191)	3.29 (2.95 to 3.67)	3.06 (2.68 to 3.49)		
Anti-7F 5 Mth post dose 2 (N=189, 191)	1.47 (1.3 to 1.66)	1.48 (1.3 to 1.68)		
Anti-7F 3 Mth post dose 3 (N=190, 190)	3.36 (3 to 3.77)	3.4 (3.04 to 3.81)		
Anti-9V 1 Mth post dose 2 (N=191, 191)	1.85 (1.6 to 2.14)	1.97 (1.72 to 2.26)		
Anti-9V 5 Mth post dose 2 (N=189, 191)	0.85 (0.75 to 0.95)	0.81 (0.72 to 0.91)		
Anti-9V 3 Mth post dose 3 (N=190, 190)	2.86 (2.54 to 3.23)	2.67 (2.32 to 3.06)		
Anti-14 1 Mth post dose 2 (N=192, 190)	2.39 (2.01 to 2.85)	2.29 (1.92 to 2.72)		
Anti-14 5 Mth post dose 2 (N=189, 191)	0.85 (0.7 to 1.03)	0.89 (0.75 to 1.06)		
Anti-14 3 Mth post dose 3 (N=190, 189)	2.4 (2.07 to 2.79)	2.42 (2.09 to 2.8)		
Anti-18C 1 Mth post dose 2 (N=191, 188)	11.33 (9.39 to 13.68)	10.88 (8.98 to 13.18)		
Anti-18C 5 Mth post dose 2 (N=189, 190)	3 (2.54 to 3.53)	3.18 (2.71 to 3.74)		
Anti-18C 3 Mth post dose 3 (N=190, 190)	18.38 (15.94 to 21.19)	16.24 (14.11 to 18.69)		
Anti-19F 1 Mth post dose 2 (N=193, 192)	7.33 (6.17 to 8.71)	7.85 (6.61 to 9.32)		
Anti-19F 5 Mth post dose 2 (N=187, 191)	2.38 (2.07 to 2.74)	2.48 (2.12 to 2.9)		
Anti-19F 3 Mth post dose 3 (N=189, 189)	5.99 (5.13 to 7.01)	6.27 (5.36 to 7.32)		
Anti-23F 1 Mth post dose 2 (N=189, 189)	0.63 (0.51 to 0.78)	0.67 (0.53 to 0.84)		
Anti-23F 5 Mth post dose 2 (N=189, 191)	0.44 (0.37 to 0.52)	0.46 (0.39 to 0.55)		
Anti-23F 3 Mth post dose 3 (N=190, 190)	1.46 (1.24 to 1.72)	1.5 (1.27 to 1.76)		

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations against vaccine serotypes 3 and 19A – For Cohort 2/Step 2 subjects who received the 3+0 Schedule

End point title	Antibody concentrations against vaccine serotypes 3 and 19A – For Cohort 2/Step 2 subjects who received the 3+0 Schedule ^[34]
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End point description:

Antibody concentrations were measured by 22F-inhibition Enzyme-Linked ImmunoSorbent Assay (ELISA), expressed as geometric mean concentrations (GMCs), in micrograms per milliliter (µg/mL). The cut-off of the assay was an antibody concentration higher than or equal to (\geq) 0.05 µg/mL. This outcome concerns subjects enrolled in Cohort 2/Step 2 who received the 3+0 Schedule.

End point type	Secondary
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End point timeframe:

At 1, 5 and 8 months (Mth) post-Dose 3 of pneumococcal vaccine administered (10PP vaccine, Synflorix™ or Prevnar 13™)

Notes:

[34] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-LD 3+0d Group	10PP-HD 3+0d Group	Synflorix 3+0d Group	Prevnar13 3+0d Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	189	192	195	192
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-3 1 Mth post dose 3 (N=184, 192, 186, 192)	0.05 (0.04 to 0.06)	0.05 (0.04 to 0.05)	0.05 (0.04 to 0.06)	4.52 (4.15 to 4.92)
Anti-3 5 Mth post dose 3 (N=189, 192, 191, 188)	0.06 (0.05 to 0.07)	0.06 (0.05 to 0.08)	0.07 (0.06 to 0.09)	0.6 (0.52 to 0.68)
Anti-3 8 Mth post dose 3 (N=188, 190, 195, 187)	0.08 (0.07 to 0.11)	0.09 (0.07 to 0.12)	0.09 (0.07 to 0.11)	0.32 (0.27 to 0.38)
Anti-19A 1 Mth post dose 3 (N=185, 190, 182, 191)	0.24 (0.2 to 0.29)	0.2 (0.17 to 0.24)	0.23 (0.19 to 0.27)	5.27 (4.41 to 6.3)
Anti-19A 5 Mth post dose 3 (N=187, 186, 194, 187)	0.21 (0.17 to 0.25)	0.17 (0.14 to 0.21)	0.24 (0.2 to 0.3)	0.91 (0.76 to 1.08)
Anti-19A 8 Mth post dose 3 (N=184, 185, 192, 185)	0.24 (0.19 to 0.29)	0.21 (0.17 to 0.27)	0.27 (0.22 to 0.34)	0.64 (0.52 to 0.79)

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations against vaccine serotypes 3 and 19A – For Cohort 2/Step 2 subjects who received the 2+1 Schedule

End point title	Antibody concentrations against vaccine serotypes 3 and 19A – For Cohort 2/Step 2 subjects who received the 2+1 Schedule ^[35]
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End point description:

Antibody concentrations were measured by 22F-inhibition Enzyme-Linked ImmunoSorbent Assay (ELISA), expressed as geometric mean concentrations (GMCs), in micrograms per milliliter (µg/mL). The cut-off of the assay was an antibody concentration higher than or equal to (\geq) 0.05 µg/mL. This outcome concerns subjects enrolled in Cohort 2/Step 2 who received the 2+1 Schedule.

End point type	Secondary
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End point timeframe:

At 1 and 5 months (Mth) post-Dose 2, and at 3 months post-Dose 3 of the pneumococcal vaccine administered (10PP vaccine or Synflorix™)

Notes:

[35] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-HD 2+1d Group	Synflorix 2+1d Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	190	191		
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-3 1 Mth post dose 2 (N=186, 187)	0.04 (0.04 to 0.05)	0.05 (0.04 to 0.06)		
Anti-3 5 Mth post dose 2 (N=187, 191)	0.06 (0.05 to 0.07)	0.07 (0.05 to 0.09)		
Anti-3 3 Mth post dose 3 (N=190, 190)	0.07 (0.06 to 0.09)	0.08 (0.06 to 0.1)		
Anti-19A 1 Mth post dose 2 (N=187, 186)	0.24 (0.2 to 0.29)	0.25 (0.2 to 0.3)		
Anti-19A 5 Mth post dose 2 (N=183, 190)	0.18 (0.15 to 0.22)	0.19 (0.15 to 0.24)		
Anti-19A 3 Mth post dose 3 (N=190, 187)	0.56 (0.43 to 0.71)	0.64 (0.5 to 0.81)		

Statistical analyses

No statistical analyses for this end point

Secondary: Titers for opsonophagocytic activity against vaccine serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F – For Cohort 2/Step 2 subjects receiving the 3+0 Schedule

End point title	Titers for opsonophagocytic activity against vaccine serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F – For Cohort 2/Step 2 subjects receiving the 3+0 Schedule ^[36]
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End point description:

The cut-off of the assay was a titer for opsonophagocytic activity higher than or equal to (\geq) 8. This outcome concerns subjects enrolled in Cohort 2/Step 2 receiving the 3+0 Schedule.

End point type	Secondary
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End point timeframe:

At 1, 5 and 8 months (Mth) post-Dose 3 of pneumococcal vaccine administered (10PP vaccine, Synflorix™ or Prevnar 13™)

Notes:

[36] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-LD 3+0d Group	10PP-HD 3+0d Group	Synflorix 3+0d Group	Prevnam13 3+0d Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	93	96	98	96
Units: Titers				
geometric mean (confidence interval 95%)				
OPSONO-1 1 Mth post dose 3 (N=93, 96, 98, 96)	136.3 (98.8 to 188)	62.7 (42.8 to 91.9)	109.9 (79.2 to 152.6)	161.4 (116.5 to 223.8)
OPSONO-1 5 Mth post dose 3 (N=93, 95, 94, 90)	14.1 (9.9 to 20)	10.1 (7.4 to 13.8)	11 (7.9 to 15.3)	14.3 (9.9 to 20.4)
OPSONO-1 8 Mth post dose 3 (N=91, 95, 96, 88)	10 (7.3 to 13.6)	8.4 (6.4 to 11)	9.3 (6.9 to 12.5)	12.5 (8.8 to 17.6)
OPSONO-4 1 Mth post dose 3 (N=91, 95, 98, 94)	835 (657.1 to 1061)	784 (633.1 to 970.8)	715.6 (586.5 to 873.2)	1022.7 (839.6 to 1245.7)
OPSONO-4 5 Mth post dose 3 (N=86, 91, 93, 84)	86 (58.5 to 126.4)	48.2 (31.5 to 73.7)	54.7 (37.2 to 80.4)	62.8 (40 to 98.4)
OPSONO-4 8 Mth post dose 3 (N=86, 90, 91, 85)	48.2 (31 to 74.9)	34.3 (21.8 to 53.9)	41.7 (27.4 to 63.7)	41.8 (25.9 to 67.5)
OPSONO-5 1 Mth post dose 3 (N=93, 95, 97, 96)	97.9 (75.5 to 127)	51.4 (37.8 to 70.1)	76.7 (58.5 to 100.6)	91.5 (69.7 to 120.2)
OPSONO-5 5 Mth post dose 3 (N=93, 96, 97, 90)	19.7 (14.9 to 26.1)	13.1 (10 to 17.3)	16.2 (12.1 to 21.5)	17.4 (13.2 to 23)
OPSONO-5 8 Mth post dose 3 (N=92, 95, 98, 89)	9.4 (7.4 to 11.9)	8.3 (6.5 to 10.5)	11.2 (8.7 to 14.2)	10.8 (8.5 to 13.6)
OPSONO-6B 1 Mth post dose 3 (N=93, 95, 96, 96)	827.6 (601.4 to 1138.9)	432.8 (293.1 to 638.8)	814.6 (594.1 to 1116.9)	1317.6 (937.1 to 1852.6)
OPSONO-6B 5 Mth post dose 3 (N=93, 91, 97, 88)	242.4 (158.9 to 369.9)	251.3 (169.1 to 373.4)	324 (227.2 to 461.9)	90.9 (53.3 to 155)
OPSONO-6B 8 Mth post dose 3 (N=90, 88, 97, 83)	146.9 (95.9 to 225.1)	126 (80.4 to 197.4)	233.1 (160.7 to 338.1)	73.7 (43.3 to 125.4)
OPSONO-7F 1 Mth post dose 3 (N=93, 95, 98, 96)	3755.3 (3060.5 to 4607.9)	2993.3 (2440.1 to 3672)	3767.9 (2981.2 to 4762.1)	7241 (5923.2 to 8852.1)
OPSONO-7F 5 Mth post dose 3 (N=93, 96, 97, 90)	2072.1 (1634.8 to 2626.3)	1850.6 (1454.8 to 2354.1)	1710.3 (1329.7 to 2199.9)	3652.1 (2878.1 to 4634.2)
OPSONO-7F 8 Mth post dose 3 (N=92, 95, 98, 89)	2001.5 (1629.3 to 2458.7)	2313 (1851.4 to 2889.8)	2291.2 (1903.9 to 2757.3)	3054.1 (2502.7 to 3727)
OPSONO-9V 1 Mth post dose 3 (N=93, 96, 98, 94)	909.2 (722.3 to 1144.5)	1113.1 (888 to 1395.3)	1044.6 (788.6 to 1383.6)	878.3 (647.7 to 1191)
OPSONO-9V 5 Mth post dose 3 (N=92, 95, 97, 90)	360.3 (253.2 to 512.7)	449.2 (347.2 to 581.3)	320.1 (236.2 to 433.6)	342.8 (240.3 to 489)
OPSONO-9V 8 Mth post dose 3 (N=89, 92, 97, 88)	330.6 (230.2 to 474.9)	436.7 (322.5 to 591.4)	277 (196.1 to 391.4)	308.6 (216.6 to 439.7)
OPSONO-14 1 Mth post dose 3 (N=93, 95, 97, 93)	1176.2 (823.1 to 1680.9)	1169.8 (845.3 to 1618.9)	1139.9 (773.2 to 1680.4)	2504.7 (1665.7 to 3766.3)
OPSONO-14 5 Mth post dose 3 (N=89, 95, 95, 89)	188.9 (129.7 to 275)	181.3 (125.6 to 261.5)	233.4 (160.2 to 340.1)	499.3 (350.5 to 711.1)
OPSONO-14 8 Mth post dose 3 (N=88, 89, 95, 89)	152.9 (103 to 227.1)	186.9 (130.5 to 267.6)	223.1 (159 to 313.2)	371 (257.6 to 534.2)
OPSONO-18C 1 Mth post dose 3 (N=93, 96, 98, 94)	666.2 (542.9 to 817.6)	532 (413.8 to 683.9)	623.6 (493.1 to 788.6)	277.7 (209.9 to 367.5)
OPSONO-18C 5 Mth post dose 3 (N=92, 95, 96, 90)	39.8 (29.4 to 54)	32 (22.9 to 44.6)	44.1 (32.7 to 59.5)	9.1 (7 to 11.8)
OPSONO-18C 8 Mth post dose 3 (N=88, 92, 97, 88)	13.6 (10.2 to 18.1)	11.7 (9 to 15.1)	16.9 (12.8 to 22.4)	6.5 (5 to 8.3)
OPSONO-19F 1 Mth post dose 3 (N=90, 95, 98, 94)	420.3 (307.6 to 574.2)	340.6 (242.7 to 478)	518.3 (389.1 to 690.4)	84.8 (66.1 to 108.9)

OPSONO-19F 5 Mth post dose 3 (N=92, 96, 98, 91)	47.2 (35.3 to 62.9)	30.7 (22.8 to 41.4)	66.9 (49.3 to 90.9)	7.2 (5.4 to 9.5)
OPSONO-19F 8 Mth post dose 3 (N=92, 94, 97, 89)	22 (16.3 to 29.6)	20.3 (14.6 to 28.5)	32.5 (23.6 to 44.7)	7 (5.4 to 9.2)
OPSONO-23F 1 Mth post dose 3 (N=93, 94, 98, 96)	1421.3 (976.4 to 2068.9)	965.1 (622.7 to 1495.8)	1030.2 (693 to 1531.4)	2821.9 (1913.1 to 4162.3)
OPSONO-23F 5 Mth post dose 3 (N=85, 87, 90, 86)	307.4 (183 to 516.3)	387.1 (234.4 to 639.1)	239.5 (140.2 to 409.1)	638.6 (369.2 to 1104.6)
OPSONO-23F 8 Mth post dose 3 (N=87, 81, 89, 83)	306.2 (172.3 to 543.9)	385.9 (221.1 to 673.5)	410.8 (246.7 to 684.2)	650.4 (367.1 to 1152.3)

Statistical analyses

No statistical analyses for this end point

Secondary: Titers for opsonophagocytic activity against vaccine serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F – For Cohort 2/Step 2 subjects receiving the 2+1 Schedule

End point title	Titers for opsonophagocytic activity against vaccine serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F – For Cohort 2/Step 2 subjects receiving the 2+1 Schedule ^[37]
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End point description:

The cut-off of the assay was a titer for opsonophagocytic activity higher than or equal to (\geq) 8. This outcome concerns subjects enrolled in Cohort 2/Step 2 receiving the 2+1 Schedule.

End point type	Secondary
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End point timeframe:

At 1 and 5 months (Mth) post-Dose 2, and at 3 months post-Dose 3 of the pneumococcal vaccine administered (10PP vaccine or Synflorix™)

Notes:

[37] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-HD 2+1d Group	Synflorix 2+1d Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	98	97		
Units: Titers				
geometric mean (confidence interval 95%)				
OPSONO-1 1 Mth post dose 2 (N=98, 97)	67.3 (46.5 to 97.4)	58 (40.4 to 83.4)		
OPSONO-1 5 Mth post dose 2 (N=95, 95)	7.7 (6 to 9.8)	8.1 (6.1 to 10.7)		
OPSONO-1 3 Mth post dose 3 (N=95, 95)	58.8 (38.2 to 90.7)	57.5 (37.8 to 87.5)		
OPSONO-4 1 Mth post dose 2 (N=97, 96)	461.9 (377.9 to 564.5)	427.2 (327 to 558)		
OPSONO-4 5 Mth post dose 2 (N=92, 90)	27 (18.6 to 39.2)	27.4 (18.6 to 40.4)		
OPSONO-4 3 Mth post dose 3 (N=93, 91)	260 (190 to 355.8)	241.1 (170.4 to 341)		

OPSONO-5 1 Mth post dose 2 (N=98, 97)	49.1 (37 to 65)	49.1 (36.2 to 66.6)		
OPSONO-5 5 Mth post dose 2 (N=95, 95)	11.8 (9.3 to 15.1)	12.6 (9.7 to 16.4)		
OPSONO-5 3 Mth post dose 3 (N=96, 95)	58.2 (44 to 77)	47 (34.4 to 64.2)		
OPSONO-6B 1 Mth post dose 2 (N=95, 96)	359.8 (240.2 to 539)	331.7 (223.1 to 493.2)		
OPSONO-6B 5 Mth post dose 2 (N=91, 91)	159.1 (102 to 248)	111.1 (68.3 to 180.7)		
OPSONO-6B 3 Mth post dose 3 (N=94, 89)	214.7 (146.2 to 315.1)	192 (130 to 283.6)		
OPSONO-7F 1 Mth post dose 2 (N=98, 96)	2643.3 (2122.6 to 3291.6)	2336.3 (1923.9 to 2837.3)		
OPSONO-7F 5 Mth post dose 2 (N=95, 94)	1258.2 (972.6 to 1627.6)	1466.4 (1150.1 to 1869.7)		
OPSONO-7F 3 Mth post dose 3 (N=96, 95)	2767.6 (2261.7 to 3386.7)	2963.6 (2379 to 3691.9)		
OPSONO-9V 1 Mth post dose 2 (N=98, 96)	783.7 (609 to 1008.5)	763.2 (625.4 to 931.4)		
OPSONO-9V 5 Mth post dose 2 (N=91, 94)	241.3 (159 to 366.2)	163.3 (113.8 to 234.3)		
OPSONO-9V 3 Mth post dose 3 (N=95, 95)	1044.3 (818.8 to 1332)	712.4 (534.2 to 950)		
OPSONO-14 1 Mth post dose 2 (N=98, 96)	349.7 (231.7 to 527.8)	310.5 (200.1 to 481.9)		
OPSONO-14 5 Mth post dose 2 (N=89, 91)	54.3 (35.5 to 83)	40.2 (26.6 to 60.8)		
OPSONO-14 3 Mth post dose 3 (N=93, 93)	335.9 (257.2 to 438.7)	254.6 (180.4 to 359.4)		
OPSONO-18C 1 Mth post dose 2 (N=98, 97)	464.7 (317 to 681.2)	459.7 (330.7 to 639.1)		
OPSONO-18C 5 Mth post dose 2 (N=93, 95)	28.4 (20.3 to 39.7)	33.6 (23.5 to 47.8)		
OPSONO-18C 3 Mth post dose 3 (N=96, 94)	562.8 (405 to 782)	522 (390 to 698.7)		
OPSONO-19F 1 Mth post dose 2 (N=96, 96)	299.3 (213.5 to 419.6)	284.7 (201.1 to 403.1)		
OPSONO-19F 5 Mth post dose 2 (N=93, 94)	35.5 (26 to 48.3)	38.7 (27.6 to 54.3)		
OPSONO-19F 3 Mth post dose 3 (N=96, 95)	203.6 (140.5 to 295.1)	168.1 (110 to 256.8)		
OPSONO-23F 1 Mth post dose 2 (N=94, 95)	539.6 (343.1 to 848.6)	493.9 (308.8 to 789.8)		
OPSONO-23F 5 Mth post dose 2 (N=90, 91)	156.5 (88.7 to 276.3)	158.6 (91.1 to 276.1)		
OPSONO-23F 3 Mth post dose 3 (N=95, 91)	612.2 (395.6 to 947.4)	835.7 (548.1 to 1274.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Titers for opsonophagocytic activity against vaccine serotypes 3 and 6A – For Cohort 2/Step 2 subjects receiving the 3+0 Schedule

End point title	Titers for opsonophagocytic activity against vaccine serotypes 3 and 6A – For Cohort 2/Step 2 subjects receiving the 3+0 Schedule ^[38]
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End point description:

The cut-off of the assay was a titer for opsonophagocytic activity higher than or equal to (\geq) 8. This outcome concerns subjects enrolled in Cohort 2/Step 2 receiving the 3+0 Schedule.

End point type	Secondary
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End point timeframe:

At 1, 5 and 8 months (Mth) post-Dose 3 of pneumococcal vaccine administered (10PP vaccine, Synflorix™ or Prevnar 13™)

Notes:

[38] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-LD 3+0d Group	10PP-HD 3+0d Group	Synflorix 3+0d Group	Prevnar13 3+0d Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	92	94	97	96
Units: Titers				
geometric mean (confidence interval 95%)				
OPSONO-3 1 Mth post dose 3 (N=92, 92, 97, 96)	5.3 (4.3 to 6.4)	4.5 (4 to 5.1)	4.8 (4.2 to 5.5)	98.3 (82.8 to 116.7)
OPSONO-3 5 Mth post dose 3 (N=91, 94, 94, 89)	7.1 (5.6 to 9)	5.5 (4.5 to 6.6)	6.7 (5.3 to 8.5)	15.1 (11 to 20.6)
OPSONO-3 8 Mth post dose 3 (N=86, 91, 95, 87)	8.1 (6.3 to 10.5)	8.3 (6.3 to 11)	7.8 (6.1 to 10.1)	12.3 (9 to 16.7)
OPSONO-6A 1 Mth post dose 3 (N=88, 91, 96, 96)	13.7 (9 to 20.9)	11.8 (8 to 17.4)	11.3 (7.7 to 16.5)	2770 (2216.1 to 3462.4)
OPSONO-6A 5 Mth post dose 3 (N=92, 92, 94, 88)	14.8 (9.5 to 23.2)	12 (8 to 17.9)	20.2 (12.7 to 32)	602 (433.4 to 836.2)
OPSONO-6A 8 Mth post dose 3 (N=86, 86, 88, 87)	14.8 (9.4 to 23.3)	12.4 (8.1 to 19.1)	18.5 (11.7 to 29.3)	260.1 (167.4 to 404.2)

Statistical analyses

No statistical analyses for this end point

Secondary: Titers for opsonophagocytic activity against vaccine serotypes 3 and 6A – For Cohort 2/Step 2 subjects receiving the 2+1 Schedule

End point title	Titers for opsonophagocytic activity against vaccine serotypes 3 and 6A – For Cohort 2/Step 2 subjects receiving the 2+1 Schedule ^[39]
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End point description:

The cut-off of the assay was a titer for opsonophagocytic activity higher than or equal to (\geq) 8. This outcome concerns subjects enrolled in Cohort 2/Step 2 receiving the 2+1 Schedule.

End point type	Secondary
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End point timeframe:

At 1 and 5 months (Mth) post-Dose 2, and at 3 months post-Dose 3 of the pneumococcal vaccine administered (10PP vaccine or Synflorix™)

Notes:

[39] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-HD 2+1d Group	Synflorix 2+1d Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	96	97		
Units: Titers				
geometric mean (confidence interval 95%)				
OPSONO-3 1 Mth post dose 2 (N=96, 97)	4.7 (4.2 to 5.4)	5.1 (4.2 to 6.1)		
OPSONO-3 5 Mth post dose 2 (N=87, 86)	5.9 (4.8 to 7.3)	5.9 (4.6 to 7.6)		
OPSONO-3 3 Mth post dose 3 (N=92, 93)	7.4 (5.7 to 9.6)	6.8 (5.4 to 8.4)		
OPSONO-6A 1 Mth post dose 2 (N=96, 97)	6.7 (5.1 to 8.8)	6.7 (5.1 to 8.7)		
OPSONO-6A 5 Mth post dose 2 (N=93, 95)	12.4 (8.4 to 18.3)	12.2 (8.2 to 18.3)		
OPSONO-6A 3 Mth post dose 3 (N=88, 91)	12.6 (8.3 to 19.2)	10 (6.7 to 15)		

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of antibodies against diphtheria (Anti-D) and tetanus (Anti-T) – For Cohort 2/Step 2 subjects receiving the 3+0 Schedule

End point title	Concentrations of antibodies against diphtheria (Anti-D) and tetanus (Anti-T) – For Cohort 2/Step 2 subjects receiving the 3+0 Schedule ^[40]
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End point description:

Seroprotection rate = Anti-D or anti-T antibody concentrations ≥ 0.1 IU/mL. This outcome concerns subjects enrolled in Cohort 2/Step 2 receiving the 3+0 Schedule.

End point type	Secondary
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End point timeframe:

At 1 month post-Dose 3 of the pneumococcal vaccine administered (10PP vaccine, Synflorix™ or Prevnar 13™)

Notes:

[40] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-LD 3+0d Group	10PP-HD 3+0d Group	Synflorix 3+0d Group	Prevnam13 3+0d Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	99	99	98	99
Units: IU/mL				
geometric mean (confidence interval 95%)				
Anti-D 1 Mth post dose 3	2.499 (2.111 to 2.959)	2.696 (2.381 to 3.053)	2.874 (2.524 to 3.272)	1.531 (1.33 to 1.762)
Anti-T 1 Mth post dose 3	4.977 (4.127 to 6.002)	5.113 (4.294 to 6.089)	4.709 (3.994 to 5.551)	4.047 (3.462 to 4.731)

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of antibodies against diphtheria (Anti-D) and tetanus (Anti-T) – For Cohort 2/Step 2 subjects receiving the 2+1 Schedule

End point title	Concentrations of antibodies against diphtheria (Anti-D) and tetanus (Anti-T) – For Cohort 2/Step 2 subjects receiving the 2+1 Schedule ^[41]
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End point description:

Seroprotection rate = Anti-D or anti-T antibody concentrations ≥ 0.1 IU/mL. This outcome concerns subjects enrolled in Cohort 2/Step 2 receiving the 2+1 Schedule.

End point type	Secondary
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End point timeframe:

At 1 month post-Dose 2 of the pneumococcal vaccine administered (10PP vaccine or Synflorix™)

Notes:

[41] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1. Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-HD 2+1d Group	Synflorix 2+1d Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95	96		
Units: IU/mL				
geometric mean (confidence interval 95%)				
Anti-D 1 Mth post dose 2	2.591 (2.213 to 3.033)	2.56 (2.207 to 2.969)		
Anti-T 1 Mth post dose 2	5.714 (4.816 to 6.781)	4.738 (3.905 to 5.749)		

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of antibodies against Bordetella pertussis (Anti-BPT) –

For Cohort 2/Step 2 subjects receiving the 3+0 Schedule

End point title	Concentrations of antibodies against Bordetella pertussis (Anti-BPT) – For Cohort 2/Step 2 subjects receiving the 3+0 Schedule ^[42]
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End point description:

Seropositivity rate = Anti-BPT concentrations \geq 15 EL.U/mL. This outcome concerns subjects enrolled in Cohort 2/Step 2 receiving the 3+0 Schedule.

End point type	Secondary
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End point timeframe:

At 1 month post-Dose 3 of the pneumococcal vaccine administered (10PP vaccine, Synflorix[™] or Prevnar 13[™])

Notes:

[42] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-LD 3+0d Group	10PP-HD 3+0d Group	Synflorix 3+0d Group	Prevnar13 3+0d Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	99	99	98	99
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-BPT 1 Mth post dose 3	111.9 (99.4 to 125.8)	110.3 (99.3 to 122.5)	105.8 (94.4 to 118.6)	117 (105 to 130.3)

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of antibodies against Bordetella pertussis (Anti-BPT) – For Cohort 2/Step 2 subjects receiving the 2+1 Schedule

End point title	Concentrations of antibodies against Bordetella pertussis (Anti-BPT) – For Cohort 2/Step 2 subjects receiving the 2+1 Schedule ^[43]
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End point description:

Seropositivity rate = Anti-BPT concentrations \geq 15 EL.U/mL. This outcome concerns subjects enrolled in Cohort 2/Step 2 receiving the 2+1 Schedule.

End point type	Secondary
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End point timeframe:

At 1 month post-Dose 2 of the pneumococcal vaccine administered (10PP vaccine or Synflorix[™])

Notes:

[43] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-HD 2+1d Group	Synflorix 2+1d Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	94	96		
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-BPT 1 Mth post dose 2	123.2 (112 to 135.5)	114.7 (101.3 to 129.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of antibodies against polyribosyl ribitol phosphate (Anti-PRP) – For Cohort 2/Step 2 subjects receiving the 3+0 Schedule

End point title	Concentrations of antibodies against polyribosyl ribitol phosphate (Anti-PRP) – For Cohort 2/Step 2 subjects receiving the 3+0 Schedule ^[44]
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End point description:

Seroprotection rate = Anti-PRP antibody concentrations ≥ 0.15 µg/mL. This outcome concerns subjects enrolled in Cohort 2/Step 2 receiving the 3+0 Schedule.

End point type	Secondary
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End point timeframe:

At 1 month post-Dose 3 of the pneumococcal vaccine administered (10PP vaccine, Synflorix™ or Prevnar 13™)

Notes:

[44] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-LD 3+0d Group	10PP-HD 3+0d Group	Synflorix 3+0d Group	Prevnar13 3+0d Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	99	99	98	99
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-PRP 1 Mth post dose 3	23.381 (19.326 to 28.287)	19.397 (15.319 to 24.561)	19.239 (15.085 to 24.537)	18.981 (15.244 to 23.635)

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of antibodies against polyribosyl ribitol phosphate (Anti-PRP) – For Cohort 2/Step 2 subjects receiving the 2+1 Schedule

End point title	Concentrations of antibodies against polyribosyl ribitol
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End point description:

Seroprotection rate = Anti-PRP antibody concentrations ≥ 0.15 µg/mL. This outcome concerns subjects enrolled in Cohort 2/Step 2 receiving the 2+1 Schedule.

End point type	Secondary
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End point timeframe:

At 1 month post-Dose 2 of the pneumococcal vaccine administered (10PP vaccine or Synflorix™)

Notes:

[45] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-HD 2+1d Group	Synflorix 2+1d Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95	96		
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-PRP 1 Mth post dose 2	21.274 (17.909 to 25.272)	21.15 (17.427 to 25.669)		

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of antibodies against hepatitis B surface antigens (Anti-HBs) – For Cohort 2/Step 2 subjects receiving the 3+0 Schedule

End point title	Concentrations of antibodies against hepatitis B surface antigens (Anti-HBs) – For Cohort 2/Step 2 subjects receiving the 3+0 Schedule ^[46]
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End point description:

Seroprotection rate = Anti-HB antibody concentrations ≥ 10 mIU/mL. This outcome concerns subjects enrolled in Cohort 2/Step 2 receiving the 3+0 Schedule.

End point type	Secondary
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End point timeframe:

At 1 month post-Dose 3 of the pneumococcal vaccine administered (10PP vaccine, Synflorix™ or Prevnar 13™)

Notes:

[46] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-LD 3+0d Group	10PP-HD 3+0d Group	Synflorix 3+0d Group	Prevnar13 3+0d Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	94	93	91	89
Units: mIU/mL				
geometric mean (confidence interval 95%)				
Anti-HBs 1 Mth post dose 3	1235.8 (946.9 to 1612.9)	1165.8 (910.7 to 1492.3)	990.1 (757.6 to 1294)	1206.6 (946.2 to 1538.7)

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of antibodies against hepatitis B surface antigens (Anti-HBs) – For Cohort 2/Step 2 subjects receiving the 2+1 Schedule

End point title	Concentrations of antibodies against hepatitis B surface antigens (Anti-HBs) – For Cohort 2/Step 2 subjects receiving the 2+1 Schedule ^[47]
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End point description:

Seroprotection rate = Anti-HB antibody concentrations ≥ 10 mIU/mL. This outcome concerns subjects enrolled in Cohort 2/Step 2 receiving the 2+1 Schedule.

End point type	Secondary
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End point timeframe:

At 1 month post-Dose 2 of the pneumococcal vaccine administered (10PP vaccine or Synflorix™)

Notes:

[47] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-HD 2+1d Group	Synflorix 2+1d Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	88		
Units: mIU/mL				
geometric mean (confidence interval 95%)				
Anti-HBs 1 Mth post dose 2	1318.5 (1062.5 to 1636.3)	976.5 (724.2 to 1316.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody titers against poliovirus 1, 2 and 3 (Anti-Polio, Anti-Polio 2 and Anti-Polio 3) – For Cohort 2/Step 2 subjects receiving the 3+0 Schedule

End point title	Antibody titers against poliovirus 1, 2 and 3 (Anti-Polio, Anti-Polio 2 and Anti-Polio 3) – For Cohort 2/Step 2 subjects
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End point description:

Seroprotection rate = Anti-Polio titres ≥ 8 . This outcome concerns subjects enrolled in Cohort 2/Step 2 receiving the 3+0 Schedule.

End point type	Secondary
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End point timeframe:

At 1 month post-Dose 3 of the pneumococcal vaccine administered (10PP vaccine, Synflorix™ or Prevnar 13™)

Notes:

[48] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-LD 3+0d Group	10PP-HD 3+0d Group	Synflorix 3+0d Group	Prevnar13 3+0d Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	97	92	91	94
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-Polio 1- 1 Mth post dose 3 (N= 97;92;91;94)	413.2 (287 to 594.9)	314.8 (202.7 to 488.7)	447.9 (278.5 to 720.1)	398.3 (256.6 to 618.3)
Anti-Polio 2- 1 Mth post dose 3 (N= 76;78;76;73)	545.8 (371.6 to 801.6)	619.5 (462 to 830.7)	514.2 (353.8 to 747.2)	536.9 (400.6 to 719.6)
Anti-Polio 3- 1 Mth post dose 3 (N= 80;88;82;84)	135.4 (91.5 to 200.5)	166 (124.5 to 221.5)	110.1 (72.5 to 167.2)	191.8 (129.4 to 284.4)

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody titers against poliovirus 1, 2 and 3 (Anti-Polio, Anti-Polio 2 and Anti-Polio 3) – For Cohort 2/Step 2 subjects receiving the 2+1 Schedule

End point title	Antibody titers against poliovirus 1, 2 and 3 (Anti-Polio, Anti-Polio 2 and Anti-Polio 3) – For Cohort 2/Step 2 subjects receiving the 2+1 Schedule ^[49]
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End point description:

Seroprotection rate = Anti-Polio titres ≥ 8 . This outcome concerns subjects enrolled in Cohort 2/Step 2 receiving the 2+1 Schedule.

End point type	Secondary
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End point timeframe:

At 1 month post-Dose 2 of the pneumococcal vaccine administered (10PP vaccine or Synflorix™)

Notes:

[49] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-HD 2+1d Group	Synflorix 2+1d Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	87	93		
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-Polio 1 - 1 Mth post dose 2 (N=87;93)	330.3 (208.6 to 523)	415.6 (286.7 to 602.6)		
Anti-Polio 2 - 1 Mth post dose 2 (N=75;82)	486.7 (319.7 to 741.1)	702.9 (529.6 to 932.8)		
Anti-Polio 3 - 1 Mth post dose 2 (N=75;80)	106.9 (71.8 to 159.1)	181.1 (131.7 to 249)		

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of antibodies against measles (Anti-Measles) - For Cohort 2/Step 2 subjects receiving the 3+0 Schedule

End point title	Concentrations of antibodies against measles (Anti-Measles) - For Cohort 2/Step 2 subjects receiving the 3+0 Schedule ^[50]
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End point description:

Seroprotection rate = Anti-Measle antibody concentrations \geq 150 mIU/mL. This outcome concerns subjects enrolled in Cohort 2/Step 2 receiving the 3+0 Schedule.

End point type	Secondary
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End point timeframe:

At 3 months (Mth) post-vaccination with Stamaril™/M-Vac™

Notes:

[50] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-LD 3+0d Group	10PP-HD 3+0d Group	Synflorix 3+0d Group	Prevnam13 3+0d Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	90	95	96	86
Units: mIU/mL				
geometric mean (confidence interval 95%)				
Anti-Measle	329.2 (272.6 to 397.5)	298.6 (254.9 to 349.8)	295.8 (237.2 to 368.8)	274.1 (227.7 to 330)

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of antibodies against measles (Anti-Measles) - For Cohort 2/Step 2 subjects receiving the 2+1 Schedule

End point title	Concentrations of antibodies against measles (Anti-Measles) - For Cohort 2/Step 2 subjects receiving the 2+1 Schedule ^[51]
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End point description:

Seroprotection rate = Anti-Measle antibody concentrations ≥ 150 mIU/mL. This outcome concerns subjects enrolled in Cohort 2/Step 2 receiving the 2+1 Schedule.

End point type	Secondary
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End point timeframe:

At 3 months (Mth) post-vaccination with Stamaril™/M-Vac™

Notes:

[51] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-HD 2+1d Group	Synflorix 2+1d Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	96	94		
Units: mIU/mL				
geometric mean (confidence interval 95%)				
Anti-Measle	284.5 (240.9 to 336)	305.9 (256.5 to 364.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Titers of antibodies against yellow fever (Anti-YF) – For Cohort 2/Step 2 subjects receiving the 3+0 Schedule

End point title	Titers of antibodies against yellow fever (Anti-YF) – For Cohort 2/Step 2 subjects receiving the 3+0 Schedule ^[52]
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End point description:

Seroprotection rate = Anti-yellow fever antibody titers ≥ 10 . This outcome concerns subjects enrolled in Cohort 2/Step 2 receiving the 3+0 Schedule.

End point type	Secondary
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End point timeframe:

At 3 months (Mth) post-vaccination with Stamaril™/M-Vac™

Notes:

[52] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-LD 3+0d Group	10PP-HD 3+0d Group	Synflorix 3+0d Group	Prevnar13 3+0d Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	97	95	97	98
Units: Titers				
geometric mean (confidence interval 95%)				

Anti-yellow fever	334 (250.6 to 445.1)	264.7 (201 to 348.5)	379.9 (293.2 to 492.2)	306.7 (242.9 to 387.3)
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Statistical analyses

No statistical analyses for this end point

Secondary: Titers of antibodies against yellow fever (Anti-YF) – For Cohort 2/Step 2 subjects receiving the 2+1 Schedule

End point title	Titers of antibodies against yellow fever (Anti-YF) – For Cohort 2/Step 2 subjects receiving the 2+1 Schedule ^[53]
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End point description:

Seroprotection rate = Anti-yellow fever antibody titers ≥ 10 . This outcome concerns subjects enrolled in Cohort 2/Step 2 receiving the 2+1 Schedule.

End point type	Secondary
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End point timeframe:

At 3 months (Mth) post-vaccination with Stamaril™/M-Vac™

Notes:

[53] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-HD 2+1d Group	Synflorix 2+1d Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	94	95		
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-yellow fever	342 (252.2 to 463.7)	239 (176 to 324.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any unsolicited adverse events (AEs) – For Step 2/Cohort 2 subjects receiving the 2+1 Schedule

End point title	Number of subjects with any unsolicited adverse events (AEs) – For Step 2/Cohort 2 subjects receiving the 2+1 Schedule ^[54]
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End point description:

An unsolicited 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. An AE can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a medicinal product. For marketed medicinal products, this also includes failure to produce expected benefits (i.e. lack of efficacy), abuse or misuse. Any = Occurrence of an unsolicited AE, regardless of intensity or relationship to vaccination. This outcome concerns Step 2/Cohort 2 subjects receiving the

2+1 Schedule.

End point type	Secondary
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End point timeframe:

Within the 31-day (Days 0-30) period post vaccination with Dose 3 of pneumococcal vaccine (10PP vaccine or Synflorix™)

Notes:

[54] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-HD 2+1d Group	Synflorix 2+1d Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	191	195		
Units: Subjects				
Any AE(s)	7	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any serious adverse events (SAEs) – For Step 2/Cohort 2 subjects receiving the 3+0 Schedule

End point title	Number of subjects with any serious adverse events (SAEs) – For Step 2/Cohort 2 subjects receiving the 3+0 Schedule ^[55]
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End point description:

SAEs assessed include medical occurrences that result in death, are life-threatening, require hospitalization or prolongation of hospitalization, result in disability/incapacity. These should also be considered serious: invasive or malignant cancers, intensive treatment in an emergency room or at home for allergic bronchospasm, blood dyscrasias or convulsions that do not result in hospitalization. Any = Occurrence of an SAE, regardless of relationship to vaccination. This outcome concerns subjects enrolled in Cohort 2/Step 2 receiving the 3+0 Schedule.

End point type	Secondary
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End point timeframe:

From Day 0 to Month 10

Notes:

[55] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-LD 3+0d Group	10PP-HD 3+0d Group	Synflorix 3+0d Group	Prevnar13 3+0d Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	200	200	200	200
Units: Subjects				
Any SAE(s)	1	4	3	2

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any serious adverse events (SAEs) – For Step 2/Cohort 2 subjects receiving the 2+1 Schedule

End point title	Number of subjects with any serious adverse events (SAEs) – For Step 2/Cohort 2 subjects receiving the 2+1 Schedule ^[56]
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End point description:

SAEs assessed include medical occurrences that result in death, are life-threatening, require hospitalization or prolongation of hospitalization, result in disability/incapacity. These should also be considered serious: invasive or malignant cancers, intensive treatment in an emergency room or at home for allergic bronchospasm, blood dyscrasias or convulsions that do not result in hospitalization. Any = Occurrence of an SAE, regardless of relationship to vaccination. This outcome concerns subjects enrolled in Cohort 2/Step 2 receiving the 2+1 Schedule.

End point type	Secondary
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End point timeframe:

From Day 0 to Month 10

Notes:

[56] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-HD 2+1d Group	Synflorix 2+1d Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	200	200		
Units: Subjects				
Any SAE(s)	4	5		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with Streptococcus pneumoniae in the nasopharynx – For Cohort 2/Step 2 subjects receiving the 3+0 Schedule

End point title	Number of subjects with Streptococcus pneumoniae in the nasopharynx – For Cohort 2/Step 2 subjects receiving the 3+0 Schedule ^[57]
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End point description:

Numbers of subjects with positive nasopharyngeal sample were calculated per group, at each swab time point. This outcome concerns subjects enrolled in Cohort 2/Step 2 receiving the 3+0 Schedule.

End point type	Secondary
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End point timeframe:

At 1, 5 and 8 months (Mth) post-Dose 3 of pneumococcal vaccine administered (10PP vaccine, Synflorix™ or Prevnar 13™)

Notes:

[57] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-LD 3+0d Group	10PP-HD 3+0d Group	Synflorix 3+0d Group	Prevnar13 3+0d Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	193	194	196	196
Units: Subjects				
At 1 Mth post dose 3 (N=193;194;196;196)	165	158	166	155
At 5 Mth post dose 3 (N=193;192;194;193)	166	161	176	168
At 8 Mth post dose 3 (N=189;189;194;191)	174	166	174	171

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with Streptococcus pneumoniae (any) in the nasopharynx – For Cohort 2/Step 2 subjects receiving the 2+1 Schedule

End point title	Number of subjects with Streptococcus pneumoniae (any) in the nasopharynx – For Cohort 2/Step 2 subjects receiving the 2+1 Schedule ^[58]
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End point description:

Numbers of subjects with positive nasopharyngeal sample were calculated per group, at each swab time point. This outcome concerns subjects enrolled in Cohort 2/Step 2 receiving the 2+1 Schedule.

End point type	Secondary
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End point timeframe:

At 1 and 5 months (Mth) post-Dose 2, and at 3 months post-Dose 3 of the pneumococcal vaccine administered (10PP vaccine or Synflorix™)

Notes:

[58] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-HD 2+1d Group	Synflorix 2+1d Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	197	197		
Units: Subjects				
At 1 Mth post-dose 2 N=(197;197)	159	162		
At 5 Mth post-dose 2 N=(189;194)	164	173		
At 3 Mths post-dose 3 N=(190;193)	178	176		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with Streptococcus pneumoniae (10Pn-PD-DiT vaccine serotypes) in the nasopharynx – For Cohort 2/Step 2 subjects receiving the 3+0 Schedule

End point title	Number of subjects with Streptococcus pneumoniae (10Pn-PD-DiT vaccine serotypes) in the nasopharynx – For Cohort 2/Step 2 subjects receiving the 3+0 Schedule ^[59]
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End point description:

Numbers of subjects with positive nasopharyngeal sample were calculated per group, at each swab time point. A Streptococcus. Pneumoniae (S. pn). vaccine pneumococcal serotype was defined as any of the pneumococcal S. pn. vaccine serotypes, e. a. serotypes 1, 3, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F. This outcome concerns subjects enrolled in Cohort 2/Step 2 receiving the 3+0 Schedule.

End point type	Secondary
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End point timeframe:

At 1, 5 and 8 months (Mth) post-Dose 3 of pneumococcal vaccine administered (10PP vaccine, Synflorix™ or Prevnar 13™)

Notes:

[59] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-LD 3+0d Group	10PP-HD 3+0d Group	Synflorix 3+0d Group	Prevnar13 3+0d Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	193	194	196	196
Units: Subjects				
At 1 Mth post dose 3 (N=193;194;196;196)	24	31	34	29
At 5 Mth post dose 3 (N=193;192;194;193)	25	23	28	30
At 8 Mth post dose 3 (N=189;189;194;191)	24	15	16	21

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with Streptococcus pneumoniae (10Pn-PD-DiT vaccine serotypes) in the nasopharynx – For Cohort 2/Step 2 subjects receiving the 2+1 Schedule

End point title	Number of subjects with Streptococcus pneumoniae (10Pn-PD-DiT vaccine serotypes) in the nasopharynx – For Cohort 2/Step
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End point description:

Numbers of subjects with positive nasopharyngeal sample were calculated per group, at each swab time point. A *Streptococcus. Pneumoniae* (S. pn). vaccine pneumococcal serotype was defined as any of the pneumococcal S. pn. vaccine serotypes, e. a. serotypes 1, 3, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F. This outcome concerns subjects enrolled in Cohort 2/Step 2 receiving the 2+1 Schedule.

End point type

Secondary

End point timeframe:

At 1 and 5 months (Mth) post-Dose 2, and at 3 months post-Dose 3 of the pneumococcal vaccine administered (10PP vaccine or Synflorix™)

Notes:

[60] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-HD 2+1d Group	Synflorix 2+1d Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	197	197		
Units: Subjects				
At 1 Mth post-dose 2 N=(197;197)	27	24		
At 5 Mth post-dose 2 N=(189;194)	24	23		
At 3 Mths post-dose 3 N=(190;193)	18	19		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with *Streptococcus pneumoniae* (Synflorix related serotypes) in the nasopharynx – For Cohort 2/Step 2 subjects receiving the 3+0 Schedule

End point title

Number of subjects with *Streptococcus pneumoniae* (Synflorix related serotypes) in the nasopharynx – For Cohort 2/Step 2 subjects receiving the 3+0 Schedule^[61]

End point description:

Related serotype = any serotype belonging to the same serogroup as the Synflorix vaccine serotypes, but different from the vaccine serotypes, was considered for the analyses of carriage of *S. pneumoniae* cross-related serotypes. This outcome concerns subjects enrolled in Cohort 2/Step 2 receiving the 3+0 Schedule.

End point type

Secondary

End point timeframe:

At 1, 5 and 8 months (Mth) post-Dose 3 of pneumococcal vaccine administered (10PP vaccine, Synflorix™ or Prevnar 13™)

Notes:

[61] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-LD 3+0d Group	10PP-HD 3+0d Group	Synflorix 3+0d Group	Prevnar13 3+0d Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	193	194	196	196
Units: Subjects				
At 1 Mth post dose 3 (N=193;194;196;196)	57	56	60	48
At 5 Mth post dose 3 (N=193;192;194;193)	54	48	58	46
At 8 Mth post dose 3 (N=189;189;194;191)	45	42	47	42

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with Streptococcus pneumoniae (Synflorix related serotypes) in the nasopharynx – For Cohort 2/Step 2 subjects receiving the 2+1 Schedule

End point title	Number of subjects with Streptococcus pneumoniae (Synflorix related serotypes) in the nasopharynx – For Cohort 2/Step 2 subjects receiving the 2+1 Schedule ^[62]
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End point description:

Related serotype = any serotype belonging to the same serogroup as the Synflorix vaccine serotypes, but different from the vaccine serotypes, was considered for the analyses of carriage of S. pneumoniae cross-related serotypes. This outcome concerns subjects enrolled in Cohort 2/Step 2 receiving the 2+1 Schedule.

End point type	Secondary
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End point timeframe:

At 1 and 5 months (Mth) post-Dose 2, and at 3 months post-Dose 3 of the pneumococcal vaccine administered (10PP vaccine or Synflorix™)

Notes:

[62] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-HD 2+1d Group	Synflorix 2+1d Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	197	197		
Units: Subjects				
At 1 Mth post-dose 2 N=(197;197)	62	50		
At 5 Mth post-dose 2 N=(189;194)	45	49		
At 3 Mths post-dose 3 N=(190;193)	58	52		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with Haemophilus influenzae in the nasopharynx – For Cohort 2/Step 2 subjects receiving the 3+0 Schedule

End point title	Number of subjects with Haemophilus influenzae in the nasopharynx – For Cohort 2/Step 2 subjects receiving the 3+0 Schedule ^[63]
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End point description:

This outcome concerns subjects enrolled in Cohort 2/Step 2 receiving the 3+0 Schedule.

End point type	Secondary
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End point timeframe:

At 1, 5 and 8 months (Mth) post-Dose 3 of pneumococcal vaccine administered (10PP vaccine, Synflorix™ or Prevnar 13™)

Notes:

[63] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-LD 3+0d Group	10PP-HD 3+0d Group	Synflorix 3+0d Group	Prevnar13 3+0d Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	193	194	195	196
Units: Subjects				
At 1 Mth post dose 3 (N=192;194;195;196)	29	33	28	37
At 5 Mth post dose 3 (N=193;192;193;193)	27	28	28	30
At 8 Mth post dose 3 (N=189;189;194;191)	9	13	12	9

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with Haemophilus influenzae in the nasopharynx – For Cohort 2/Step 2 subjects receiving the 2+1 Schedule

End point title	Number of subjects with Haemophilus influenzae in the nasopharynx – For Cohort 2/Step 2 subjects receiving the 2+1 Schedule ^[64]
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End point description:

This outcome concerns subjects enrolled in Cohort 2/Step 2 receiving the 2+1 Schedule.

End point type	Secondary
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End point timeframe:

At 1 and 5 months (Mth) post-Dose 2, and at 3 months post-Dose 3 of the pneumococcal vaccine administered (10PP vaccine or Synflorix™)

Notes:

[64] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-HD 2+1d Group	Synflorix 2+1d Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	197	197		
Units: Subjects				
At 1 Mth post-dose 2 N=(197;197)	26	23		
At 5 Mth post-dose 2 N=(187;194)	20	32		
At 3 Mths post-dose 3 N=(190;193)	9	11		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with Moraxella catarrhalis in the nasopharynx – For Cohort 2/Step 2 subjects receiving the 3+0 Schedule

End point title	Number of subjects with Moraxella catarrhalis in the nasopharynx – For Cohort 2/Step 2 subjects receiving the 3+0 Schedule ^[65]
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End point description:

Positive cultures of other bacterial pathogens [such as S. aureus, Streptococcus pyogenes (Group A streptococci) and Moraxella catarrhalis] identified in the nasopharynx were analyzed. This outcome concerns subjects enrolled in Cohort 2/Step 2 receiving the 3+0 Schedule.

End point type	Secondary
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End point timeframe:

At 1, 5 and 8 months (Mth) post-Dose 3 of pneumococcal vaccine administered (10PP vaccine, Synflorix™ or Prevnar 13™)

Notes:

[65] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-LD 3+0d Group	10PP-HD 3+0d Group	Synflorix 3+0d Group	Prevnar13 3+0d Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	193	194	196	196
Units: Subjects				
At 1 Mth post dose 3 (N=193;194;196;196)	88	98	104	100
At 5 Mth post dose 3 (N=193;192;194;193)	72	73	78	88
At 8 Mth post dose 3 (N=189;189;194;191)	74	67	70	74

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with Moraxella catarrhalis in the nasopharynx – For

Cohort 2/Step 2 subjects receiving the 2+1 Schedule

End point title	Number of subjects with Moraxella catarrhalis in the nasopharynx – For Cohort 2/Step 2 subjects receiving the 2+1 Schedule ^[66]
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End point description:

Positive cultures of other bacterial pathogens [such as S. aureus, Streptococcus pyogenes (Group A streptococci) and Moraxella catarrhalis] identified in the nasopharynx were analyzed. This outcome concerns subjects enrolled in Cohort 2/Step 2 receiving the 2+1 Schedule.

End point type	Secondary
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End point timeframe:

At 1 and 5 months (Mth) post-Dose 2, and at 3 months post-Dose 3 of the pneumococcal vaccine administered (10PP vaccine or Synflorix™)

Notes:

[66] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-HD 2+1d Group	Synflorix 2+1d Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	197	197		
Units: Subjects				
At 1 Mth post-dose 2 N=(197;197)	86	93		
At 5 Mth post-dose 2 N=(189;194)	73	84		
At 3 Mths post-dose 3 N=(190;193)	56	83		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with Group A Streptococcus in the nasopharynx – For Cohort 2/Step 2 subjects receiving the 3+0 Schedule

End point title	Number of subjects with Group A Streptococcus in the nasopharynx – For Cohort 2/Step 2 subjects receiving the 3+0 Schedule ^[67]
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End point description:

Positive cultures of other bacterial pathogens [such as S. aureus, Streptococcus pyogenes (Group A streptococci) and Moraxella catarrhalis] identified in the nasopharynx were analyzed. This outcome concerns subjects enrolled in Cohort 2/Step 2 receiving the 3+0 Schedule.

End point type	Secondary
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End point timeframe:

At 1, 5 and 8 months (Mth) post-Dose 3 of pneumococcal vaccine administered (10PP vaccine, Synflorix™ or Prevnar 13™)

Notes:

[67] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-LD 3+0d Group	10PP-HD 3+0d Group	Synflorix 3+0d Group	Prevnar13 3+0d Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	193	194	196	196
Units: Subjects				
At 1 Mth post dose 3 (N=193;194;196;196)	5	4	5	4
At 5 Mth post dose 3 (N=193;192;194;193)	4	3	4	1
At 8 Mth post dose 3 (N=189;189;194;191)	4	6	7	6

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with Group A Streptococcus in the nasopharynx – For Cohort 2/Step 2 subjects receiving the 2+1 Schedule

End point title	Number of subjects with Group A Streptococcus in the nasopharynx – For Cohort 2/Step 2 subjects receiving the 2+1 Schedule ^[68]
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End point description:

Positive cultures of other bacterial pathogens [such as *S. aureus*, *Streptococcus pyogenes* (Group A streptococci) and *Moraxella catarrhalis*] identified in the nasopharynx were analyzed. This outcome concerns subjects enrolled in Cohort 2/Step 2 receiving the 2+1 Schedule.

End point type	Secondary
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End point timeframe:

At 1 and 5 months (Mth) post-Dose 2, and at 3 months post-Dose 3 of the pneumococcal vaccine administered (10PP vaccine or Synflorix™)

Notes:

[68] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-HD 2+1d Group	Synflorix 2+1d Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	197	197		
Units: Subjects				
At 1 Mth post-dose 2 N=(197;197)	6	4		
At 5 Mth post-dose 2 N=(189;194)	2	4		
At 3 Mths post-dose 3 N=(190;193)	5	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with Staphylococcus aureus in the nasopharynx –

For Cohort 2/Step 2 subjects receiving the 3+0 Schedule

End point title	Number of subjects with Staphylococcus aureus in the nasopharynx – For Cohort 2/Step 2 subjects receiving the 3+0 Schedule ^[69]
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End point description:

Positive cultures of other bacterial pathogens [such as *S. aureus*, *Streptococcus pyogenes* (Group A streptococci) and *Moraxella catarrhalis*] identified in the nasopharynx were analyzed. This outcome concerns subjects enrolled in Cohort 2/Step 2 receiving the 3+0 Schedule.

End point type	Secondary
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End point timeframe:

At 1, 5 and 8 months (Mth) post-Dose 3 of pneumococcal vaccine administered (10PP vaccine, Synflorix™ or Prevnar 13™)

Notes:

[69] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-LD 3+0d Group	10PP-HD 3+0d Group	Synflorix 3+0d Group	Prevnar13 3+0d Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	193	194	196	196
Units: Subjects				
At 1 Mth post dose 3 (N=193;194;196;196)	44	44	54	50
At 5 Mth post dose 3 (N=193;192;194;193)	36	37	39	37
At 8 Mth post dose 3 (N=189;189;194;191)	13	17	25	11

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with Staphylococcus aureus in the nasopharynx – For Cohort 2/Step 2 subjects receiving the 2+1 Schedule

End point title	Number of subjects with Staphylococcus aureus in the nasopharynx – For Cohort 2/Step 2 subjects receiving the 2+1 Schedule ^[70]
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End point description:

Positive cultures of other bacterial pathogens [such as *S. aureus*, *Streptococcus pyogenes* (Group A streptococci) and *Moraxella catarrhalis*] identified in the nasopharynx were analyzed. This outcome concerns subjects enrolled in Cohort 2/Step 2 receiving the 2+1 Schedule.

End point type	Secondary
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End point timeframe:

At 1 and 5 months (Mth) post-Dose 2, and at 3 months post-Dose 3 of the pneumococcal vaccine administered (10PP vaccine or Synflorix™)

Notes:

[70] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-HD 2+1d Group	Synflorix 2+1d Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	197	197		
Units: Subjects				
At 1 Mth post-dose 2 N=(197;197)	46	62		
At 5 Mth post-dose 2 N=(189;194)	32	40		
At 3 Mths post-dose 3 N=(190;193)	21	17		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with acquisition of non-vaccine serotypes/serogroups of Streptococcus pneumoniae in the nasopharynx – For Cohort 2/Step 2 subjects receiving the 3+0 Schedule

End point title	Number of subjects with acquisition of non-vaccine serotypes/serogroups of Streptococcus pneumoniae in the nasopharynx – For Cohort 2/Step 2 subjects receiving the 3+0 Schedule ^[71]
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End point description:

This outcome concerns subjects enrolled in Cohort 2/Step 2 receiving the 3+0 Schedule.

End point type	Secondary
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End point timeframe:

At 1, 5 and 8 months (Mth) post-Dose 3 of pneumococcal vaccine administered (10PP vaccine or Synflorix™)

Notes:

[71] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-LD 3+0d Group	10PP-HD 3+0d Group	Synflorix 3+0d Group	Prevnar13 3+0d Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	193	194	196	196
Units: Subjects				
At 1 Mth post dose 3 (N=193;194;196;196)	124	106	120	112
At 5 Mth post dose 3 (N=192;191;194;191)	108	122	131	126
At 8 Mth post dose 3 (N=189;189;193;190)	121	115	122	122

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with acquisition of non-vaccine

serotypes/serogroups of Streptococcus pneumoniae in the nasopharynx – For Cohort 2/Step 2 subjects receiving the 2+1 Schedule

End point title	Number of subjects with acquisition of non-vaccine serotypes/serogroups of Streptococcus pneumoniae in the nasopharynx – For Cohort 2/Step 2 subjects receiving the 2+1 Schedule ^[72]
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End point description:

This outcome concerns subjects enrolled in Cohort 2/Step 2 receiving the 2+1 Schedule.

End point type	Secondary
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End point timeframe:

At 1 and 5 months (Mth) post-Dose 2, and at 3 months post-Dose 3 of the pneumococcal vaccine administered (10PP vaccine or Synflorix™)

Notes:

[72] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-HD 2+1d Group	Synflorix 2+1d Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	197	197		
Units: Subjects				
At 1 Mth post-dose 2 N=(197;197)	117	128		
At 5 Mth post-dose 2 N=(189;193)	119	138		
At 3 Mths post-dose 3 N=(188;192)	129	117		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with acquisition of any new Streptococcus pneumoniae in the nasopharynx – For Cohort 2/Step 2 subjects receiving the 3+0 Schedule

End point title	Number of subjects with acquisition of any new Streptococcus pneumoniae in the nasopharynx – For Cohort 2/Step 2 subjects receiving the 3+0 Schedule ^[73]
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End point description:

This outcome concerns subjects enrolled in Cohort 2/Step 2 receiving the 3+0 Schedule.

End point type	Secondary
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End point timeframe:

At 1, 5 and 8 months (Mth) post-Dose 3 of pneumococcal vaccine administered (10PP vaccine or Synflorix™)

Notes:

[73] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-LD 3+0d Group	10PP-HD 3+0d Group	Synflorix 3+0d Group	Prevnar13 3+0d Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	193	194	196	196
Units: Subjects				
At 1 Mth post dose 3 (N=193;194;196;196)	136	130	142	133
At 5 Mth post dose 3 (N=192;191;194;191)	128	130	145	142
At 8 Mth post dose 3 (N=189;189;193;190)	139	128	136	135

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with acquisition of any new Streptococcus pneumoniae in the nasopharynx – For Cohort 2/Step 2 subjects receiving the 2+1 Schedule

End point title	Number of subjects with acquisition of any new Streptococcus pneumoniae in the nasopharynx – For Cohort 2/Step 2 subjects receiving the 2+1 Schedule ^[74]
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End point description:

This outcome concerns subjects enrolled in Cohort 2/Step 2 receiving the 2+1 Schedule.

End point type	Secondary
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End point timeframe:

At 1 and 5 months (Mth) post-Dose 2, and at 3 months post-Dose 3 of the pneumococcal vaccine administered (10PP vaccine or Synflorix™)

Notes:

[74] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-HD 2+1d Group	Synflorix 2+1d Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	197	197		
Units: Subjects				
At 1 Mth post-dose 2 N=(197;197)	136	141		
At 5 Mth post-dose 2 N=(189;193)	136	155		
At 3 Mths post-dose 3 N=(188;192)	144	131		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with acquisition of Haemophilus influenzae with Polymerase Chain Reaction differentiation in the nasopharynx – For Cohort 2/Step 2

subjects receiving the 3+0 Schedule

End point title	Number of subjects with acquisition of Haemophilus influenzae with Polymerase Chain Reaction differentiation in the nasopharynx – For Cohort 2/Step 2 subjects receiving the 3+0 Schedule ^[75]
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End point description:

This outcome concerns subjects enrolled in Cohort 2/Step 2 receiving the 3+0 Schedule.

End point type	Secondary
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End point timeframe:

At 1, 5 and 8 months (Mth) post-Dose 3 of pneumococcal vaccine administered (10PP vaccine or Synflorix™)

Notes:

[75] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-LD 3+0d Group	10PP-HD 3+0d Group	Synflorix 3+0d Group	Prevnar13 3+0d Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	193	194	196	196
Units: Subjects				
At 1 Mth post dose 3 (N=193;194;196;196)	17	21	16	19
At 5 Mth post dose 3 (N=192;191;194;191)	24	23	25	24
At 8 Mth post dose 3 (N=189;189;193;190)	9	10	10	6

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with acquisition of Haemophilus influenzae with Polymerase Chain Reaction differentiation in the nasopharynx – For Cohort 2/Step 2 subjects receiving the 2+1 Schedule

End point title	Number of subjects with acquisition of Haemophilus influenzae with Polymerase Chain Reaction differentiation in the nasopharynx – For Cohort 2/Step 2 subjects receiving the 2+1 Schedule ^[76]
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End point description:

This outcome concerns subjects enrolled in Cohort 2/Step 2 receiving the 2+1 Schedule.

End point type	Secondary
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End point timeframe:

At 1 and 5 months (Mth) post-Dose 2, and at 3 months post-Dose 3 of the pneumococcal vaccine administered (10PP vaccine or Synflorix™)

Notes:

[76] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-HD 2+1d Group	Synflorix 2+1d Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	197	197		
Units: Subjects				
At 1 Mth post-dose 2 (N=197;197)	12	12		
At 5 Mth post-dose 2 (N=189;193)	20	25		
At 3 Mth post-dose 3 (N=188;192)	9	8		

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations against vaccine serotype 6A – For Cohort 2/Step 2 subjects who received the 3+0 Schedule

End point title	Antibody concentrations against vaccine serotype 6A – For Cohort 2/Step 2 subjects who received the 3+0 Schedule ^[77]
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End point description:

Antibody concentrations were measured by 22F-inhibition Enzyme-Linked ImmunoSorbent Assay (ELISA), expressed as geometric mean concentrations (GMCs), in micrograms per milliliter (µg/mL). The cut-off of the assay was an antibody concentration higher than or equal to (\geq) 0.05 µg/mL. This outcome concerns subjects enrolled in Cohort 2/Step 2 who received the 3+0 Schedule.

End point type	Secondary
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End point timeframe:

At 1, 5 and 8 months (Mth) post-Dose 3 of pneumococcal vaccine administered (10PP vaccine, Synflorix™ or Prevnar 13™)

Notes:

[77] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-LD 3+0d Group	10PP-HD 3+0d Group	Synflorix 3+0d Group	Prevnar13 3+0d Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	190	192	192	190
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-6A 1Mth post dose 3(N=185,192,187,190)	0.13 (0.11 to 0.16)	0.13 (0.11 to 0.15)	0.13 (0.11 to 0.15)	3.01 (2.60 to 3.48)
Anti-6A 5 Mth post dose 3(N=190,190,192,189)	0.17 (0.14 to 0.20)	0.15 (0.13 to 0.18)	0.22 (0.18 to 0.27)	1.0 (0.89 to 1.13)
Anti-6A 8 Mth post dose 3(N=177,179,178,148)	0.16 (0.14 to 0.19)	0.15 (0.13 to 0.18)	0.18 (0.15 to 0.22)	0.59 (0.51 to 0.68)

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations against vaccine serotype 6A – For Cohort 2/Step 2 subjects who received the 2+1 Schedule

End point title	Antibody concentrations against vaccine serotype 6A – For Cohort 2/Step 2 subjects who received the 2+1 Schedule ^[78]
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End point description:

Antibody concentrations were measured by 22F-inhibition Enzyme-Linked ImmunoSorbent Assay (ELISA), expressed as geometric mean concentrations (GMCs), in micrograms per milliliter (µg/mL). The cut-off of the assay was an antibody concentration higher than or equal to (\geq) 0.05 µg/mL. This outcome concerns subjects enrolled in Cohort 2/Step 2 who received the 2+1 Schedule.

End point type	Secondary
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End point timeframe:

At 1 and 5 months (Mth) post-Dose 2, and at 3 months post-Dose 3 of the pneumococcal vaccine administered (10PP vaccine or Synflorix™)

Notes:

[78] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1. Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-HD 2+1d Group	Synflorix 2+1d Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	187	189		
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-6A 1 Mth post dose 2(N=187, 187)	0.11 (0.09 to 0.12)	0.11 (0.09 to 0.13)		
Anti-6A 5 Mth post-dose 2(N=185, 189)	0.10 (0.09 to 0.12)	0.12 (0.10 to 0.14)		
Anti-6A 3 Mth post dose 3(N=174, 175)	0.14 (0.12 to 0.16)	0.15 (0.12 to 0.17)		

Statistical analyses

No statistical analyses for this end point

Secondary: Titers for opsonophagocytic activity against vaccine serotype 19A – For Cohort 2/Step 2 subjects receiving the 3+0 Schedule

End point title	Titers for opsonophagocytic activity against vaccine serotype 19A – For Cohort 2/Step 2 subjects receiving the 3+0 Schedule ^[79]
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End point description:

The cut-off of the assay was a titer for opsonophagocytic activity higher than or equal to (\geq) to the serotype-specific Lower Limit of Quantification (= 143). This outcome concerns subjects enrolled in Cohort 2/Step 2 receiving the 3+0 Schedule.

End point type	Secondary
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End point timeframe:

At 1, 5 and 8 months (Mth) post-Dose 3 of pneumococcal vaccine administered (10PP vaccine, Synflorix™ or Prevnar 13™)

Notes:

[79] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-LD 3+0d Group	10PP-HD 3+0d Group	Synflorix 3+0d Group	Prevnam13 3+0d Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	71	79	71	89
Units: Titers				
geometric mean (confidence interval 95%)				
OPSONO-19A 1 Mth post dose 3 (N=70,72,71,89)	347.0 (238.0 to 505.9)	281.1 (192.8 to 409.8)	369.8 (257.5 to 531.0)	2652.8 (2277.5 to 3089.9)
OPSONO-19A 5 Mth post dose 3 (N=71,75,61,69)	120.4 (91.9 to 157.8)	121.6 (94.3 to 156.8)	140.2 (102.1 to 192.4)	704.2 (498.5 to 994.8)
OPSONO-19A 8 Mth post dose 3 (N=67,79,69,60)	155.2 (109.1 to 220.9)	151.5 (110.0 to 208.7)	138.7 (101.3 to 190.0)	394.4 (261.8 to 594.2)

Statistical analyses

No statistical analyses for this end point

Secondary: Titers for opsonophagocytic activity against vaccine serotype 19A – For Cohort 2/Step 2 subjects receiving the 2+1 Schedule

End point title	Titers for opsonophagocytic activity against vaccine serotype 19A – For Cohort 2/Step 2 subjects receiving the 2+1 Schedule ^[80]
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End point description:

The cut-off of the assay was a titer for opsonophagocytic activity higher than or equal to (\geq) to the serotype-specific Lower Limit of Quantification (= 143). This outcome concerns subjects enrolled in Cohort 2/Step 2 receiving the 2+1 Schedule.

End point type	Secondary
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End point timeframe:

At 1 and 5 months (Mth) post-Dose 2, and at 3 months post-Dose 3 of the pneumococcal vaccine administered (10PP vaccine or Synflorix™)

Notes:

[80] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-HD 2+1d Group	Synflorix 2+1d Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	72	81		
Units: Titers				
geometric mean (confidence interval 95%)				
OPSONO-19A 1 Mth post dose 2 (N=69,71)	231.3 (164.5 to 325.4)	177.4 (129.4 to 243.2)		
OPSONO-19A 5 Mth post dose 2 (N=67,81)	99.1 (80.0 to 122.7)	107.4 (84.5 to 136.5)		

OPSONO-19A 3 Mth post dose 3 (N=72,79)	274.2 (187.6 to 400.8)	361.2 (247.5 to 527.2)		
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Statistical analyses

No statistical analyses for this end point

Other pre-specified: Description of Non-Vaccine-Type S.pneumoniae samples isolated from Nasopharyngeal swabs before and after vaccination for the Ply gene – Cohort 2

End point title	Description of Non-Vaccine-Type S.pneumoniae samples isolated from Nasopharyngeal swabs before and after vaccination for the Ply gene – Cohort 2
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End point description:

Isolates from the Prev13_3D group were not selected. Samples were distributed evenly in the 5 groups and across time points: 10 isolates from pre-vaccination, 20 at Month 3, 20 at Month 7 and 20 at Month 10. Only samples displaying non-vaccine and non-vaccine related serotypes (all serotypes except serotypes 1, 4, 5 and 14 and serotypes belonging to the serogroups 6, 7, 9, 18, 19 and 23) were selected in systematic (equal number across groups) but non-random manner. Samples were described as follows: samples with gene detected (Positive isolates) with sequenced protein, number of protein Variants, number of isolates with Variant 1 (100% identity with vaccine sequence).

End point type	Other pre-specified
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End point timeframe:

At Month 0 (Pre-vaccination), Month 3 (1 month [m] post-dose [P] III-3+0 schedule or PII-2+1 schedule), Month 7 (5 m PIII - 3+0 schedule or PII-2+1 schedule) or at Month 10 (8 m PIII - 3+0 schedule or 3 m post-booster-2+1 schedule)

End point values	Total "all 5" Group			
Subject group type	Subject analysis set			
Number of subjects analysed	350			
Units: Samples				
Positive isolates	347			
Protein sequenced	347			
Protein variants	18			
Samples with Variant 1	216			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Description of Non-Vaccine-Type S.pneumoniae samples isolated from Nasopharyngeal swabs before and after vaccination for the PhtD gene – Cohort 2

End point title	Description of Non-Vaccine-Type S.pneumoniae samples isolated from Nasopharyngeal swabs before and after vaccination for the PhtD gene – Cohort 2
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End point description:

Isolates from the Prev13_3D group were not selected. Samples were distributed evenly in the 5 groups and across time points: 10 isolates from pre-vaccination, 20 at Month 3, 20 at Month 7 and 20 at Month 10. Only samples displaying non-vaccine and non-vaccine related serotypes (all serotypes except serotypes 1, 4, 5 and 14 and serotypes belonging to the serogroups 6, 7, 9, 18, 19 and 23) were selected in systematic (equal number across groups) but non-random manner. Samples were described as follows: samples with gene detected (Positive isolates) with sequenced protein, number of protein Variants, number of isolates with Variant 1 (100% identity with vaccine sequence).

End point type	Other pre-specified
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End point timeframe:

At Month 0 (Pre-vaccination), Month 3 (1 month [m] post-dose [P] III-3+0 schedule or PII-2+1 schedule), Month 7 (5 m PIII - 3+0 schedule or PII-2+1 schedule) or at Month 10 (8 m PIII - 3+0 schedule or 3 m post-booster-2+1 schedule)

End point values	Total "all 5" Group			
Subject group type	Subject analysis set			
Number of subjects analysed	350			
Units: Samples				
Positive isolates	342			
Protein sequenced	321			
Protein variants	84			
Samples with Variant 1	1			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of samples with Ply protein variants classified by number of Amino Acids (AA) mutation versus vaccine sequence in a subset of Non-Vaccine-Type S.pneumoniae isolates from Nasopharyngeal swabs – Cohort 2

End point title	Number of samples with Ply protein variants classified by number of Amino Acids (AA) mutation versus vaccine sequence in a subset of Non-Vaccine-Type S.pneumoniae isolates from Nasopharyngeal swabs – Cohort 2 ^[81]
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End point description:

Overall, 18 different Ply protein sequences were identified: 5 protein variants previously described (e.g. variants 1, 2, 7, 11 and 15), plus 13 new protein variants which are referred to as variants GSK21 to GSK33. The number of Amino Acids (AA) mutation versus vaccine sequence has been specified for each Ply variant.

The samples without gene detected were considered as negative for Ply (Ply negative).

End point type	Other pre-specified
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End point timeframe:

At Month 0 (Pre-vaccination), Month 3 (1 month [m] post-dose [P] III-3+0 schedule or PII-2+1 schedule), Month 7 (5 m PIII - 3+0 schedule or PII-2+1 schedule) and Month 10 (8 m PIII - 3+0 schedule or 3 m post-booster-2+1 schedule)

Notes:

[81] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-LD 3+0d Group	10PP-HD 3+0d Group	Synflorix 3+0d Group	10PP-HD 2+1d Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	20	20	20
Units: Samples				
Variant 1 - AA = 0 at Month 0 (N=10;10;10;10;10)	5	8	7	4
Variant 2 - AA = 1 at Month 0	4	0	1	4
Variant 15 - AA = 1 at Month 0	1	0	0	2
Variant GSK24 - AA = 1 at Month 0	0	0	1	0
Variant GSK28 - AA = 1 at Month 0	0	0	1	0
Variant GSK33-AA = 3 at Month 0 (N=10;10;10;10;10)	0	0	0	0
Variant GSK30-AA = 4 at Month 0 (N=10;10;10;10;10)	0	1	0	0
Variant GSK31-AA = 6 at Month 0 (N=10;10;10;10;10)	0	1	0	0
Ply negative at Month 0 (N=10;10;10;10;10)	0	0	0	0
Variant 1 - AA = 0 at Month 3 (N=20;20;20;20;20)	11	13	10	14
Variant 2 - AA = 1 at Month 3 (N=20;20;20;20;20)	4	7	6	4
Variant 15 - AA = 1 at Month 3 (N=20;20;20;20;20)	2	0	2	1
Variant GSK24-AA = 1 at Month 3 (N=20;20;20;20;20)	2	0	1	1
Variant 11 - AA = 2 at Month 3 (N=20;20;20;20;20)	0	0	0	0
Variant GSK23-AA = 2 at Month 3 (N=20;20;20;20;20)	0	0	0	0
Ply negative at Month 3 (N=20;20;20;20;20)	1	0	1	0
Variant 1-AA = 0 at Month 7 (N=20;20;20;20;20)	14	15	10	13
Variant 2-AA = 1 at Month 7 (N=20;20;20;20;20)	4	4	6	4
Variant 15-AA = 1 at Month 7 (N=20;20;20;20;20)	2	0	1	1
Variant GSK24-AA = 1 at Month 7 (N=20;20;20;20;20)	0	0	0	1
Variant GSK29-AA = 1 at Month 7 (N=20;20;20;20;20)	0	0	0	0
Variant 7 - AA = 2 at Month 7 (N=20;20;20;20;20)	0	1	1	1
Variant GSK21-AA = 2 at Month 7 (N=20;20;20;20;20)	0	0	1	0
Variant GSK23-AA = 2 at Month 7 (N=20;20;20;20;20)	0	0	0	0
Variant GSK27-AA = 2 at Month 7 (N=20;20;20;20;20)	0	0	1	0
Ply negative at Month 7 (N=20;20;20;20;20)	0	0	0	0
Variant 1 - AA = 0 at Month 10 (N=20;20;20;20;20)	12	15	12	12
Variant 2 - AA = 1 at Month 10 (N=20;20;20;20;20)	5	2	6	5
Variant 15 - AA = 1 at Month 10 (N=20;20;20;20;20)	1	1	0	2
Variant GSK24-AA = 1 at Month 10(N=20;20;20;20;20)	0	0	0	0

Variant GSK25-AA = 1 at Month 10(N=20;20;20;20;20)	0	1	0	0
Variant 7 - AA = 2 at Month 10 (N=20;20;20;20;20)	1	0	0	1
Variant GSK22-AA = 2 at Month 10(N=20;20;20;20;20)	0	0	1	0
Variant GSK26-AA = 4 at Month 10(N=20;20;20;20;20)	0	0	1	0
Variant GSK32-AA = 7 at Month 10(N=20;20;20;20;20)	1	0	0	0
Ply negative at Month 10 (N=20;20;20;20;20)	0	1	0	0

End point values	Synflorix 2+1d Group			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: Samples				
Variant 1 - AA = 0 at Month 0 (N=10;10;10;10;10)	8			
Variant 2 - AA = 1 at Month 0	1			
Variant 15 - AA = 1 at Month 0	0			
Variant GSK24 - AA = 1 at Month 0	0			
Variant GSK28 - AA = 1 at Month 0	0			
Variant GSK33-AA = 3 at Month 0 (N=10;10;10;10;10)	1			
Variant GSK30-AA = 4 at Month 0 (N=10;10;10;10;10)	0			
Variant GSK31-AA = 6 at Month 0 (N=10;10;10;10;10)	0			
Ply negative at Month 0 (N=10;10;10;10;10)	0			
Variant 1 - AA = 0 at Month 3 (N=20;20;20;20;20)	9			
Variant 2 - AA = 1 at Month 3 (N=20;20;20;20;20)	8			
Variant 15 - AA = 1 at Month 3 (N=20;20;20;20;20)	0			
Variant GSK24-AA = 1 at Month 3 (N=20;20;20;20;20)	0			
Variant 11 - AA = 2 at Month 3 (N=20;20;20;20;20)	1			
Variant GSK23-AA = 2 at Month 3 (N=20;20;20;20;20)	2			
Ply negative at Month 3 (N=20;20;20;20;20)	0			
Variant 1-AA = 0 at Month 7 (N=20;20;20;20;20)	10			
Variant 2-AA = 1 at Month 7 (N=20;20;20;20;20)	7			
Variant 15-AA = 1 at Month 7 (N=20;20;20;20;20)	1			
Variant GSK24-AA = 1 at Month 7 (N=20;20;20;20;20)	0			
Variant GSK29-AA = 1 at Month 7 (N=20;20;20;20;20)	1			

Variant 7 - AA = 2 at Month 7 (N=20;20;20;20;20)	0			
Variant GSK21-AA = 2 at Month 7 (N=20;20;20;20;20)	0			
Variant GSK23-AA = 2 at Month 7 (N=20;20;20;20;20)	1			
Variant GSK27-AA = 2 at Month 7 (N=20;20;20;20;20)	0			
Ply negative at Month 7 (N=20;20;20;20;20)	0			
Variant 1 - AA = 0 at Month 10 (N=20;20;20;20;20)	14			
Variant 2 - AA = 1 at Month 10 (N=20;20;20;20;20)	4			
Variant 15 - AA = 1 at Month 10 (N=20;20;20;20;20)	1			
Variant GSK24-AA = 1 at Month 10 (N=20;20;20;20;20)	1			
Variant GSK25-AA = 1 at Month 10 (N=20;20;20;20;20)	0			
Variant 7 - AA = 2 at Month 10 (N=20;20;20;20;20)	0			
Variant GSK22-AA = 2 at Month 10 (N=20;20;20;20;20)	0			
Variant GSK26-AA = 4 at Month 10 (N=20;20;20;20;20)	0			
Variant GSK32-AA = 7 at Month 10 (N=20;20;20;20;20)	0			
Ply negative at Month 10 (N=20;20;20;20;20)	0			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage (median and mean) of protein identity relative to amino acid sequence of Ply protein in the vaccine for a subset of Non-Vaccine-Type S.pneumoniae isolates from Nasopharyngeal swabs – Cohort 2

End point title	Percentage (median and mean) of protein identity relative to amino acid sequence of Ply protein in the vaccine for a subset of Non-Vaccine-Type S.pneumoniae isolates from Nasopharyngeal swabs – Cohort 2 ^[82]
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End point description:

Protein sequence identity was compared to vaccine sequence. Mean and median was calculated and expressed as percentage.

End point type	Other pre-specified
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End point timeframe:

At Month 0 (Pre-vaccination), Month 3 (1 month [m] post-dose [P] III-3+0 schedule or PII-2+1 schedule), Month 7 (5 m PIII - 3+0 schedule or PII-2+1 schedule) and Month 10 (8 m PIII - 3+0 schedule or 3 m post-booster-2+1 schedule)

Notes:

[82] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-LD 3+0d Group	10PP-HD 3+0d Group	Synflorix 3+0d Group	10PP-HD 2+1d Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	20	20	20
Units: Percentage of protein identity				
number (not applicable)				
Median at Month 0 (N=10;10;10;10;10)	99.9	100	100	99.79
Mean at Month 0 (N=10;10;10;10;10)	99.9	99.79	99.94	99.87
Median at Month 3 (N=19;20;19;20;20)	100	100	100	100
Mean at Month 3 (N=19;20;19;20;20)	99.91	99.93	99.9	99.94
Median at Month 7 (N=20;20;20;20;20)	100	100	99.9	100
Mean at Month 7 (N=20;20;20;20;20)	99.94	99.94	99.86	99.92
Median at Month 10 (N=20;19;20;20;20)	100	100	100	100
Mean at Month 10 (N=20;19;20;20;20)	99.84	99.95	99.87	99.91

End point values	Synflorix 2+1d Group			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: Percentage of protein identity				
number (not applicable)				
Median at Month 0 (N=10;10;10;10;10)	100			
Mean at Month 0 (N=10;10;10;10;10)	99.92			
Median at Month 3 (N=19;20;19;20;20)	99.79			
Mean at Month 3 (N=19;20;19;20;20)	99.85			
Median at Month 7 (N=20;20;20;20;20)	99.9			
Mean at Month 7 (N=20;20;20;20;20)	99.88			
Median at Month 10 (N=20;19;20;20;20)	100			
Mean at Month 10 (N=20;19;20;20;20)	99.94			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of samples with PhtD protein variants in a subset of Non-Vaccine-Type S.pneumoniae isolates from Nasopharyngeal swabs – Cohort 2

End point title	Number of samples with PhtD protein variants in a subset of Non-Vaccine-Type S.pneumoniae isolates from Nasopharyngeal swabs – Cohort 2 ^[83]
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End point description:

Because of high variants heterogeneity in each group (no major variant), the impact of vaccination on variant prevalence was not analysed.

PhtD sequences were detected in some samples but no consensus sequence could be obtained they were defined as mixed sequences (Mix).

The samples without gene detected were considered as negative for PhtD (PhtD negative).

End point type	Other pre-specified
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End point timeframe:

At Month 0 (Pre-vaccination), Month 3 (1 month [m] post-dose [P] III-3+0 schedule or PII-2+1

schedule), Month 7 (5 m PIII - 3+0 schedule or PII-2+1 schedule) and Month 10 (8 m PIII - 3+0 schedule or 3 m post-booster-2+1 schedule)

Notes:

[83] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-LD 3+0d Group	10PP-HD 3+0d Group	Synflorix 3+0d Group	10PP-HD 2+1d Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	20	20	20
Units: Samples				
Variants number at Month 0 (N=10;10;10;10;10)	10	6	9	9
Mix number at Month 0 (N=10;10;10;10;10)	0	1	1	0
PhtD negative at Month 0 (N=10;10;10;10;10)	0	2	0	1
Variants number at Month 3 (N=20;20;20;20;20)	16	16	18	16
Mix number at Month 3 (N=20;20;20;20;20)	1	1	0	3
PhtD negative at Month 3 (N=20;20;20;20;20)	1	0	1	0
Variants number at Month 7 (N=20;20;20;20;20)	13	14	17	13
Mix number at Month 7 (N=20;20;20;20;20)	0	2	1	1
PhtD negative at Month 7 (N=20;20;20;20;20)	0	0	0	0
Variants number at Month 10 (N=20;20;20;20;20)	13	12	13	15
Mix number at Month 10 (N=20;20;20;20;20)	1	0	1	1
PhtD negative at Month 10 (N=20;20;20;20;20)	1	1	0	0

End point values	Synflorix 2+1d Group			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: Samples				
Variants number at Month 0 (N=10;10;10;10;10)	7			
Mix number at Month 0 (N=10;10;10;10;10)	2			
PhtD negative at Month 0 (N=10;10;10;10;10)	1			
Variants number at Month 3 (N=20;20;20;20;20)	16			
Mix number at Month 3 (N=20;20;20;20;20)	1			
PhtD negative at Month 3 (N=20;20;20;20;20)	0			

Variants number at Month 7 (N=20;20;20;20;20)	12			
Mix number at Month 7 (N=20;20;20;20;20)	1			
PhtD negative at Month 7 (N=20;20;20;20;20)	0			
Variants number at Month 10 (N=20;20;20;20;20)	11			
Mix number at Month 10 (N=20;20;20;20;20)	3			
PhtD negative at Month 10 (N=20;20;20;20;20)	0			

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Percentage (median and mean) of protein identity relative to amino acid sequence of PhtD protein in the vaccine for a subset of Non-Vaccine-Type S.pneumoniae isolates from Nasopharyngeal swabs – Cohort 2

End point title	Percentage (median and mean) of protein identity relative to amino acid sequence of PhtD protein in the vaccine for a subset of Non-Vaccine-Type S.pneumoniae isolates from Nasopharyngeal swabs – Cohort 2 ^[84]
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End point description:

Protein sequence identity was compared to vaccine sequence. Mean and median was calculated and expressed as percentage.

End point type	Other pre-specified
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End point timeframe:

At Month 0 (Pre-vaccination), Month 3 (1 month [m] post-dose [P] III-3+0 schedule or PII-2+1 schedule), Month 7 (5 m PIII - 3+0 schedule or PII-2+1 schedule) and Month 10 (8 m PIII - 3+0 schedule or 3 m post-booster-2+1 schedule)

Notes:

[84] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-LD 3+0d Group	10PP-HD 3+0d Group	Synflorix 3+0d Group	10PP-HD 2+1d Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	19	19	19
Units: Percentage of protein identity number (not applicable)				
Median at Month 0 (N=10;7;9;9;7)	96.3	96.7	95.8	96.7
Mean at Month 0 (N=10;7;9;9;7)	95.2	97	96.7	96.3
Median at Month 3 (N=18;19;19;17;19)	96.6	97.7	96.6	96.3
Mean at Month 3 (N=18;19;19;17;19)	96.4	97.4	96.2	94.6
Median at Month 7 (N=20;18;19;19;19)	97.6	96.2	97.4	97.6
Mean at Month 7 (N=20;18;19;19;19)	96.7	95.6	95.7	96.7
Median at Month 10 (N=18;19;19;19;17)	97.2	97.6	96.8	96.9
Mean at Month 10 (N=18;19;19;19;17)	95.5	97.3	94.1	95.4

End point values	Synflorix 2+1d Group			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: Percentage of protein identity				
number (not applicable)				
Median at Month 0 (N=10;7;9;9;7)	95.7			
Mean at Month 0 (N=10;7;9;9;7)	96.3			
Median at Month 3 (N=18;19;19;17;19)	95.7			
Mean at Month 3 (N=18;19;19;17;19)	93.1			
Median at Month 7 (N=20;18;19;19;19)	95.7			
Mean at Month 7 (N=20;18;19;19;19)	94.7			
Median at Month 10 (N=18;19;19;19;17)	97.6			
Mean at Month 10 (N=18;19;19;19;17)	94.9			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited symptoms during the 4-day post-vaccination period in Cohort 1 and 2. Unsolicited AEs during 31-day post-vaccination period in Cohort 1 and 2. SAEs from Month 0 to Month 6 in Cohort 1 and from Month 0 to Month 10 in Cohort 2.

Adverse event reporting additional description:

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

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	18.1
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Reporting groups

Reporting group title	10PP-HD 3+0d Group
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Reporting group description:

This group consisted in infants aged 8-10 weeks at first vaccination enrolled as part the Cohort 2/Step 2 of the study who received 3 doses of the GSK 2189242A (or 10PP) vaccine in its high-dose (HD) formulation and EPI vaccines according to a 3+0 Schedule. That is, subjects received 3 doses of the 10PP vaccine, HD formulation, co-administered with the Tritanrix™-HepB/Hib and Polio Sabin™ at 2-3-4 months of age (Day 0, Month 1 and Month 2), followed by one dose of each of the M-Vac™, Stamaril™ and Polio Sabin™ vaccines administered at approximately 9 months of age. The 10PP vaccine was administered intramuscularly into the right thigh; Tritanrix™-HepB/Hib, M-Vac™ and Stamaril™ were administered intramuscularly into the left thigh; Polio Sabin™ was administered orally.

Reporting group title	Synflorix 3+0d Group
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Reporting group description:

This group consisted in infants aged 8-10 weeks at first vaccination enrolled as part the Cohort 2/Step 2 of the study who received 3 doses of Synflorix™ and EPI vaccines according to a 3+0 Schedule. That is, subjects received 3 doses of the Synflorix™, co-administered with Tritanrix™-HepB/Hib and Polio Sabin™ at 2-3-4 months of age (Day 0, Month 1 and Month 2), followed by one dose of each of the M-Vac™, Stamaril™ and Polio Sabin™ vaccines administered at approximately 9 months of age. Synflorix™ was administered intramuscularly into the right thigh; Tritanrix™-HepB/Hib, M-Vac™ and Stamaril™ were administered intramuscularly into the left thigh; Polio Sabin™ was administered orally.

Reporting group title	Synflorix 2+1d Group
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Reporting group description:

This group consisted in infants aged 8-10 weeks at first vaccination enrolled as part the Cohort 2/Step 2 of the study who received Synflorix™ and EPI vaccines according to a 2+1 Schedule. That is, subjects received 2 doses of the Synflorix™ co-administered with Tritanrix™-Hep B/Hib and Polio Sabin™ at 2-4 months of age (at Day 0 and Month 2), followed by a third dose of Synflorix™ co-administered with M-Vac™, Stamaril™ and Polio Sabin™ at approximately 9 months of age. The 2nd doses of Tritanrix™-Hep B/Hib and Polio Sabin™ in EPI vaccines were administered without any pneumococcal vaccine at 3 months of age. Synflorix™ was administered intramuscularly into the right thigh; Tritanrix™-HepB/Hib, M-Vac™ and Stamaril™ were administered intramuscularly into the left thigh; Polio Sabin™ was administered orally.

Reporting group title	Prevnar 13 3+0d Group
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Reporting group description:

This group consisted in infants aged 8-10 weeks at first vaccination enrolled as part the Cohort 2/Step 2 of the study who received 3 doses of Prevnar 13™ and EPI vaccines according to a 3+0 Schedule. That is, subjects received 3 doses of Prevnar 13™, co-administered with Tritanrix™-HepB/Hib and Polio Sabin™ at 2-3-4 months of age (Day 0, Month 1 and Month 2), followed by one dose of each of the M-Vac™, Stamaril™ and Polio Sabin™ vaccines administered at approximately 9 months of age. Prevnar 13™ was administered intramuscularly into the right thigh; Tritanrix™-HepB/Hib, M-Vac™ and Stamaril™ were administered intramuscularly into the left thigh; Polio Sabin™ was administered orally.

Reporting group title	10PP-HD 2+1d Group
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Reporting group description:

This group consisted in infants aged 8-10 weeks at first vaccination enrolled as part the Cohort 2/Step 2 of the study who received the GSK 2189242A (or 10PP) vaccine, in its high-dose (HD) formulation, and EPI vaccines according to a 2+1 Schedule. That is, subjects received 2 doses of the 10PP vaccine, HD

formulation co-administered with Tritanrix™-Hep B/Hib and Polio Sabin™ at 2-4 months of age (at Day 0 and Month 2), followed by a third dose of the same formulation co-administered with M-Vac™, Stamaril™ and Polio Sabin™ at approximately 9 months of age.. The 2nd doses of Tritanrix™-Hep B/Hib and Polio Sabin™ in EPI vaccines were administered without any pneumococcal vaccine at 3 months of age. The 10PP vaccine was administered intramuscularly into the right thigh; Tritanrix™-HepB/Hib, M-Vac™ and Stamaril™ were administered intramuscularly into the left thigh; Polio Sabin™ was administered orally.

Reporting group title	10PP-HD 1d Group
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Reporting group description:

Group This group consisted in children aged 2-4 years at vaccination enrolled as part of the Cohort 1/Step 1 of the study who received a single dose of the GSK 2189242A (or 10PP) vaccine in its high-dose (HD) formulation at Day 0. The 10PP vaccine was administered intramuscularly in the non-dominant deltoid.

Reporting group title	10PP-LD 3+0d Group
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Reporting group description:

This group consisted in infants aged 8-10 weeks at first vaccination enrolled as part the Cohort 2/Step 2 of the study who received 3 doses of the GSK 2189242A (or 10PP) vaccine in its low-dose (LD) formulation and EPI vaccines according to a 3+0 Schedule. That is, subjects received 3 doses of the 10PP vaccine, LD formulation, co-administered with Tritanrix™-HepB/Hib and Polio Sabin™ at 2-3-4 months of age (Day 0, Month 1 and Month 2), followed by one dose of each of the M-Vac™, Stamaril™ and Polio Sabin™ vaccines administered at approximately 9 months of age. The 10PP vaccine was administered intramuscularly into the right thigh; Tritanrix™-HepB/Hib, M-Vac™ and Stamaril™ were administered intramuscularly into the left thigh; Polio Sabin™ was administered orally.

Reporting group title	Prevnam 13 1d Group
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Reporting group description:

This group consisted in children aged 2-4 years at vaccination enrolled as part of the Cohort 1/Step 1 of the study who received a single dose of Prevnam 13™ at Day 0. Prevnam 13™ was administered intramuscularly in the non-dominant deltoid.

Serious adverse events	10PP-HD 3+0d Group	Synflorix 3+0d Group	Synflorix 2+1d Group
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 200 (2.00%)	3 / 200 (1.50%)	5 / 200 (2.50%)
number of deaths (all causes)	1	0	1
number of deaths resulting from adverse events			
Nervous system disorders			
Febrile convulsion			
subjects affected / exposed	0 / 200 (0.00%)	0 / 200 (0.00%)	1 / 200 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Sudden infant death syndrome			
subjects affected / exposed	0 / 200 (0.00%)	0 / 200 (0.00%)	0 / 200 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pneumonia aspiration			

subjects affected / exposed	1 / 200 (0.50%)	0 / 200 (0.00%)	0 / 200 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 200 (0.50%)	2 / 200 (1.00%)	0 / 200 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	1 / 200 (0.50%)	0 / 200 (0.00%)	1 / 200 (0.50%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Sepsis			
subjects affected / exposed	0 / 200 (0.00%)	1 / 200 (0.50%)	1 / 200 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchiolitis			
subjects affected / exposed	1 / 200 (0.50%)	0 / 200 (0.00%)	1 / 200 (0.50%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 200 (0.00%)	0 / 200 (0.00%)	1 / 200 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malaria			
subjects affected / exposed	0 / 200 (0.00%)	0 / 200 (0.00%)	0 / 200 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis bacterial			
subjects affected / exposed	1 / 200 (0.50%)	0 / 200 (0.00%)	0 / 200 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Prevnar 13 3+0d	10PP-HD 2+1d	10PP-HD 1d Group
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	Group	Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 200 (1.00%)	4 / 200 (2.00%)	0 / 60 (0.00%)
number of deaths (all causes)	2	2	0
number of deaths resulting from adverse events			
Nervous system disorders			
Febrile convulsion			
subjects affected / exposed	0 / 200 (0.00%)	0 / 200 (0.00%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Sudden infant death syndrome			
subjects affected / exposed	0 / 200 (0.00%)	1 / 200 (0.50%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pneumonia aspiration			
subjects affected / exposed	0 / 200 (0.00%)	0 / 200 (0.00%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 200 (0.50%)	2 / 200 (1.00%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 200 (0.00%)	1 / 200 (0.50%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Sepsis			
subjects affected / exposed	1 / 200 (0.50%)	0 / 200 (0.00%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Bronchiolitis			

subjects affected / exposed	0 / 200 (0.00%)	0 / 200 (0.00%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 200 (0.00%)	0 / 200 (0.00%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malaria			
subjects affected / exposed	0 / 200 (0.00%)	0 / 200 (0.00%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis bacterial			
subjects affected / exposed	0 / 200 (0.00%)	0 / 200 (0.00%)	0 / 60 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	10PP-LD 3+0d Group	Prevnar 13 1d Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 200 (0.50%)	0 / 60 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Nervous system disorders			
Febrile convulsion			
subjects affected / exposed	0 / 200 (0.00%)	0 / 60 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Sudden infant death syndrome			
subjects affected / exposed	0 / 200 (0.00%)	0 / 60 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pneumonia aspiration			

subjects affected / exposed	0 / 200 (0.00%)	0 / 60 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 200 (0.00%)	0 / 60 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	0 / 200 (0.00%)	0 / 60 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 200 (0.00%)	0 / 60 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchiolitis			
subjects affected / exposed	0 / 200 (0.00%)	0 / 60 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	0 / 200 (0.00%)	0 / 60 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaria			
subjects affected / exposed	1 / 200 (0.50%)	0 / 60 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis bacterial			
subjects affected / exposed	0 / 200 (0.00%)	0 / 60 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	10PP-HD 3+0d Group	Synflorix 3+0d Group	Synflorix 2+1d Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	191 / 200 (95.50%)	193 / 200 (96.50%)	184 / 200 (92.00%)
Nervous system disorders			
Somnolence-Cohort2:3+0 schedule			
subjects affected / exposed	46 / 200 (23.00%)	38 / 200 (19.00%)	0 / 200 (0.00%)
occurrences (all)	46	38	0
Somnolence-Cohort2:2+1 schedule- first 2 doses			
subjects affected / exposed	0 / 200 (0.00%)	0 / 200 (0.00%)	44 / 200 (22.00%)
occurrences (all)	0	0	44
Somnolence-Cohort2:2+1 schedule- third dose			
subjects affected / exposed ^[1]	0 / 200 (0.00%)	0 / 200 (0.00%)	4 / 195 (2.05%)
occurrences (all)	0	0	4
General disorders and administration site conditions			
Fever (axillary temperature $\geq 37.5^{\circ}$ C) (1 dose Group)			
subjects affected / exposed	0 / 200 (0.00%)	0 / 200 (0.00%)	0 / 200 (0.00%)
occurrences (all)	0	0	0
Pain-Cohort2:3+0 schedule			
subjects affected / exposed	121 / 200 (60.50%)	123 / 200 (61.50%)	0 / 200 (0.00%)
occurrences (all)	121	123	0
Swelling-Cohort2:3+0 schedule			
subjects affected / exposed	45 / 200 (22.50%)	40 / 200 (20.00%)	0 / 200 (0.00%)
occurrences (all)	45	40	0
Pain-Cohort2:2+1 schedule-first 2 doses			
subjects affected / exposed	0 / 200 (0.00%)	0 / 200 (0.00%)	102 / 200 (51.00%)
occurrences (all)	0	0	102
Swelling-Cohort2:2+1 schedule-first 2 doses			
subjects affected / exposed	0 / 200 (0.00%)	0 / 200 (0.00%)	31 / 200 (15.50%)
occurrences (all)	0	0	31
Pain-Cohort2:2+1 schedule-third dose			

subjects affected / exposed ^[2] occurrences (all)	0 / 200 (0.00%) 0	0 / 200 (0.00%) 0	26 / 195 (13.33%) 26
Pyrexia-Cohort 2:3+0 schedule subjects affected / exposed occurrences (all)	104 / 200 (52.00%) 104	106 / 200 (53.00%) 106	0 / 200 (0.00%) 0
Pyrexia-Cohort2:2+1 schedule-first 2 doses subjects affected / exposed occurrences (all)	0 / 200 (0.00%) 0	0 / 200 (0.00%) 0	89 / 200 (44.50%) 89
Pyrexia-Cohort2:2+1 schedule-third dose subjects affected / exposed ^[3] occurrences (all)	0 / 200 (0.00%) 0	0 / 200 (0.00%) 0	27 / 195 (13.85%) 27
Psychiatric disorders Irritability-Cohort2:3+0 schedule subjects affected / exposed occurrences (all)	133 / 200 (66.50%) 133	141 / 200 (70.50%) 141	0 / 200 (0.00%) 0
Irritability-Cohort2:2+1 schedule-first 2 doses subjects affected / exposed occurrences (all)	0 / 200 (0.00%) 0	0 / 200 (0.00%) 0	128 / 200 (64.00%) 128
Irritability-Cohort2:2+1 schedule-third dose subjects affected / exposed ^[4] occurrences (all)	0 / 200 (0.00%) 0	0 / 200 (0.00%) 0	19 / 195 (9.74%) 19
Infections and infestations Respiratory tract infection-Cohort 1 subjects affected / exposed occurrences (all)	0 / 200 (0.00%) 0	0 / 200 (0.00%) 0	0 / 200 (0.00%) 0
Respiratory tract infection-Cohort2:3+0 schedule subjects affected / exposed occurrences (all)	68 / 200 (34.00%) 68	80 / 200 (40.00%) 80	0 / 200 (0.00%) 0
Upper respiratory tract infection-Cohort2:3+0 schedule subjects affected / exposed occurrences (all)	14 / 200 (7.00%) 14	12 / 200 (6.00%) 12	0 / 200 (0.00%) 0
Respiratory tract infection-Cohort2:2+1 schedule-first 2 doses			

subjects affected / exposed occurrences (all)	0 / 200 (0.00%) 0	0 / 200 (0.00%) 0	58 / 200 (29.00%) 58
Conjunctivitis-Cohort2:3+0 schedule subjects affected / exposed occurrences (all)	4 / 200 (2.00%) 4	10 / 200 (5.00%) 10	0 / 200 (0.00%) 0
Metabolism and nutrition disorders Decreased appetite-Cohort2:3+0 schedule subjects affected / exposed occurrences (all)	30 / 200 (15.00%) 30	27 / 200 (13.50%) 27	0 / 200 (0.00%) 0
Decreased appetite-Cohort2:2+1 schedule-first 2 doses subjects affected / exposed occurrences (all)	0 / 200 (0.00%) 0	0 / 200 (0.00%) 0	25 / 200 (12.50%) 25

Non-serious adverse events	Prevnar 13 3+0d Group	10PP-HD 2+1d Group	10PP-HD 1d Group
Total subjects affected by non-serious adverse events subjects affected / exposed	188 / 200 (94.00%)	189 / 200 (94.50%)	9 / 60 (15.00%)
Nervous system disorders Somnolence-Cohort2:3+0 schedule subjects affected / exposed occurrences (all)	44 / 200 (22.00%) 44	0 / 200 (0.00%) 0	0 / 60 (0.00%) 0
Somnolence-Cohort2:2+1 schedule-first 2 doses subjects affected / exposed occurrences (all)	0 / 200 (0.00%) 0	47 / 200 (23.50%) 47	0 / 60 (0.00%) 0
Somnolence-Cohort2:2+1 schedule-third dose subjects affected / exposed ^[1] occurrences (all)	0 / 200 (0.00%) 0	12 / 191 (6.28%) 12	0 / 60 (0.00%) 0
General disorders and administration site conditions Fever (axillary temperature $\geq 37.5^{\circ}$ C) (1 dose Group) subjects affected / exposed occurrences (all)	0 / 200 (0.00%) 0	0 / 200 (0.00%) 0	4 / 60 (6.67%) 4
Pain-Cohort2:3+0 schedule subjects affected / exposed occurrences (all)	115 / 200 (57.50%) 115	0 / 200 (0.00%) 0	0 / 60 (0.00%) 0
Swelling-Cohort2:3+0 schedule			

subjects affected / exposed	37 / 200 (18.50%)	0 / 200 (0.00%)	0 / 60 (0.00%)
occurrences (all)	37	0	0
Pain-Cohort2:2+1 schedule-first 2 doses			
subjects affected / exposed	0 / 200 (0.00%)	97 / 200 (48.50%)	0 / 60 (0.00%)
occurrences (all)	0	97	0
Swelling-Cohort2:2+1 schedule-first 2 doses			
subjects affected / exposed	0 / 200 (0.00%)	35 / 200 (17.50%)	0 / 60 (0.00%)
occurrences (all)	0	35	0
Pain-Cohort2:2+1 schedule-third dose			
subjects affected / exposed ^[2]	0 / 200 (0.00%)	21 / 191 (10.99%)	0 / 60 (0.00%)
occurrences (all)	0	21	0
Pyrexia-Cohort 2:3+0 schedule			
subjects affected / exposed	106 / 200 (53.00%)	0 / 200 (0.00%)	0 / 60 (0.00%)
occurrences (all)	106	0	0
Pyrexia-Cohort2:2+1 schedule-first 2 doses			
subjects affected / exposed	0 / 200 (0.00%)	93 / 200 (46.50%)	0 / 60 (0.00%)
occurrences (all)	0	93	0
Pyrexia-Cohort2:2+1 schedule-third dose			
subjects affected / exposed ^[3]	0 / 200 (0.00%)	32 / 191 (16.75%)	0 / 60 (0.00%)
occurrences (all)	0	32	0
Psychiatric disorders			
Irritability-Cohort2:3+0 schedule			
subjects affected / exposed	136 / 200 (68.00%)	0 / 200 (0.00%)	0 / 60 (0.00%)
occurrences (all)	136	0	0
Irritability-Cohort2:2+1 schedule-first 2 doses			
subjects affected / exposed	0 / 200 (0.00%)	131 / 200 (65.50%)	0 / 60 (0.00%)
occurrences (all)	0	131	0
Irritability-Cohort2:2+1 schedule-third dose			
subjects affected / exposed ^[4]	0 / 200 (0.00%)	27 / 191 (14.14%)	0 / 60 (0.00%)
occurrences (all)	0	27	0
Infections and infestations			

Respiratory tract infection-Cohort 1 subjects affected / exposed	0 / 200 (0.00%)	0 / 200 (0.00%)	5 / 60 (8.33%)
occurrences (all)	0	0	5
Respiratory tract infection-Cohort2: 3+0 schedule			
subjects affected / exposed	80 / 200 (40.00%)	0 / 200 (0.00%)	0 / 60 (0.00%)
occurrences (all)	80	0	0
Upper respiratory tract infection- Cohort2:3+0 schedule			
subjects affected / exposed	10 / 200 (5.00%)	0 / 200 (0.00%)	0 / 60 (0.00%)
occurrences (all)	10	0	0
Respiratory tract infection-Cohort2: 2+1 schedule-first 2 doses			
subjects affected / exposed	0 / 200 (0.00%)	56 / 200 (28.00%)	0 / 60 (0.00%)
occurrences (all)	0	56	0
Conjunctivitis-Cohort2:3+0 schedule			
subjects affected / exposed	6 / 200 (3.00%)	0 / 200 (0.00%)	0 / 60 (0.00%)
occurrences (all)	6	0	0
Metabolism and nutrition disorders			
Decreased appetite-Cohort2:3+0 schedule			
subjects affected / exposed	34 / 200 (17.00%)	0 / 200 (0.00%)	0 / 60 (0.00%)
occurrences (all)	34	0	0
Decreased appetite-Cohort2:2+1 schedule-first 2 doses			
subjects affected / exposed	0 / 200 (0.00%)	24 / 200 (12.00%)	0 / 60 (0.00%)
occurrences (all)	0	24	0

Non-serious adverse events	10PP-LD 3+0d Group	Prevnar 13 1d Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	186 / 200 (93.00%)	3 / 60 (5.00%)	
Nervous system disorders			
Somnolence-Cohort2:3+0 schedule			
subjects affected / exposed	43 / 200 (21.50%)	0 / 60 (0.00%)	
occurrences (all)	43	0	
Somnolence-Cohort2:2+1 schedule- first 2 doses			
subjects affected / exposed	0 / 200 (0.00%)	0 / 60 (0.00%)	
occurrences (all)	0	0	
Somnolence-Cohort2:2+1 schedule- third dose			

subjects affected / exposed ^[1]	0 / 200 (0.00%)	0 / 60 (0.00%)	
occurrences (all)	0	0	
General disorders and administration site conditions			
Fever (axillary temperature $\geq 37.5^{\circ}\text{C}$) (1 dose Group)			
subjects affected / exposed	0 / 200 (0.00%)	2 / 60 (3.33%)	
occurrences (all)	0	2	
Pain-Cohort2:3+0 schedule			
subjects affected / exposed	108 / 200 (54.00%)	0 / 60 (0.00%)	
occurrences (all)	108	0	
Swelling-Cohort2:3+0 schedule			
subjects affected / exposed	30 / 200 (15.00%)	0 / 60 (0.00%)	
occurrences (all)	30	0	
Pain-Cohort2:2+1 schedule-first 2 doses			
subjects affected / exposed	0 / 200 (0.00%)	0 / 60 (0.00%)	
occurrences (all)	0	0	
Swelling-Cohort2:2+1 schedule-first 2 doses			
subjects affected / exposed	0 / 200 (0.00%)	0 / 60 (0.00%)	
occurrences (all)	0	0	
Pain-Cohort2:2+1 schedule-third dose			
subjects affected / exposed ^[2]	0 / 200 (0.00%)	0 / 60 (0.00%)	
occurrences (all)	0	0	
Pyrexia-Cohort 2:3+0 schedule			
subjects affected / exposed	105 / 200 (52.50%)	0 / 60 (0.00%)	
occurrences (all)	105	0	
Pyrexia-Cohort2:2+1 schedule-first 2 doses			
subjects affected / exposed	0 / 200 (0.00%)	0 / 60 (0.00%)	
occurrences (all)	0	0	
Pyrexia-Cohort2:2+1 schedule-third dose			
subjects affected / exposed ^[3]	0 / 200 (0.00%)	0 / 60 (0.00%)	
occurrences (all)	0	0	
Psychiatric disorders			

Irritability-Cohort2:3+0 schedule subjects affected / exposed occurrences (all)	139 / 200 (69.50%) 139	0 / 60 (0.00%) 0	
Irritability-Cohort2:2+1 schedule- first 2 doses subjects affected / exposed occurrences (all)	0 / 200 (0.00%) 0	0 / 60 (0.00%) 0	
Irritability-Cohort2:2+1 schedule- third dose subjects affected / exposed ^[4] occurrences (all)	0 / 200 (0.00%) 0	0 / 60 (0.00%) 0	
<p>Infections and infestations</p> <p>Respiratory tract infection-Cohort 1 subjects affected / exposed occurrences (all)</p> <p>Respiratory tract infection-Cohort2: 3+0 schedule subjects affected / exposed occurrences (all)</p> <p>Upper respiratory tract infection- Cohort2:3+0 schedule subjects affected / exposed occurrences (all)</p> <p>Respiratory tract infection-Cohort2: 2+1 schedule-first 2 doses subjects affected / exposed occurrences (all)</p> <p>Conjunctivitis-Cohort2:3+0 schedule subjects affected / exposed occurrences (all)</p>	<p>0 / 200 (0.00%) 0</p> <p>80 / 200 (40.00%) 80</p> <p>12 / 200 (6.00%) 12</p> <p>0 / 200 (0.00%) 0</p> <p>6 / 200 (3.00%) 6</p>	<p>1 / 60 (1.67%) 1</p> <p>0 / 60 (0.00%) 0</p> <p>0 / 60 (0.00%) 0</p> <p>0 / 60 (0.00%) 0</p>	
<p>Metabolism and nutrition disorders</p> <p>Decreased appetite-Cohort2:3+0 schedule subjects affected / exposed occurrences (all)</p> <p>Decreased appetite-Cohort2:2+1 schedule-first 2 doses subjects affected / exposed occurrences (all)</p>	<p>32 / 200 (16.00%) 32</p> <p>0 / 200 (0.00%) 0</p>	<p>0 / 60 (0.00%) 0</p> <p>0 / 60 (0.00%) 0</p>	

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: The analysis of the solicited symptom included only subjects with documented data.

[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: The analysis of the solicited symptom included only subjects with documented data.

[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: The analysis of the solicited symptom included only subjects with documented data.

[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: The analysis of the solicited symptom included only subjects with documented data.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 October 2010	<ul style="list-style-type: none"> - Following comments from Scientific Committee in the Gambia the inclusion/exclusion criteria were modified as follows: <ul style="list-style-type: none"> The criterion of gestational age has been removed from the inclusion criteria as the exact duration of pregnancy is difficult to retrieve in this population; Reference to HIV infection has been removed from the exclusion criteria. - In addition follow-up period of solicited adverse events has been shortened from 7 days (Day 0 - Day 6) to 4 days (Day 0 - Day 3) following vaccination in order to adjust to the scheduled field workers' visits and due to the difficulty to collect information in this population retrospectively for day 4 and day 5, when no field worker visit is performed. Consequently, field worker visits at day 6 have been removed.
10 March 2011	<ul style="list-style-type: none"> - Following advice from IDMC, the following change has been implemented: Safety analysis that will lead to a decision to begin enrolment in Cohort 2 will be done on all enrolled children from cohort 1 (approximately 120 subjects) instead of the first 60 enrolled subjects. In addition, the following changes have been included: <ul style="list-style-type: none"> - OPA assay testing techniques have been broadened by inclusion of OPA multiplex to OPA standard testing. Multiplex assay will be used in this study and future studies as it allows multiple measurements in one single test, so it would result in reduction in sera volume needed for OPA in future studies. Likewise, a multiplex immunochemistry assay with equivalent characteristics to the 22F-inhibition ELISA assay and bridged to the 22F-inhibition ELISA might be used in this study. - As a result of assay qualification, the cut-off for the functional assay measuring the inhibition of pneumolysin haemolysis activity was changed to 140 instead of 6. Quantitative serotype-specific Polymerase Chain Reaction was added to the list of bacterial diagnosis testing on the nasopharyngeal swabs that may be done if specific validated assays become available in the GSK Biologicals laboratory or a validated laboratory designated by GSK Biologicals or deemed necessary should the results of this study and/or another study require it or for development of new assays regarding the diseases or vaccines under evaluation.
06 October 2011	<ul style="list-style-type: none"> - In order to comply with the national immunisation program, a dose of OPV was to be administered to subjects from Cohort 2, at the time of Visit 5 (at approximately 9 months of age). - Vaccines such as Polio, Measles or Meningococcal Vaccines that are recommended as part of national campaigns for immunisation were now allowed to be administered at any time during the study. - Complementary analysis of immunogenicity of co-administered vaccines depending on number of received doses has been envisaged. - In the microbiological assessment section the possibility to perform additional testing on the nasopharyngeal swabs for viral pathogens has been added. - Some inconsistencies in protocol wording that could lead to misinterpretation have been clarified throughout the document.
19 June 2012	<ul style="list-style-type: none"> - At the European Medicines Agency's (EMA) request, GSK Biologicals has updated its procedure for emergency unblinding during the conduct of a clinical study. - According to the revised procedure, the responsibility and the decision to break the treatment code in emergency situations resides solely with the investigator and consequently, the investigator will have full authority to break the treatment code. - The anti-PD, anti-Ply, anti-PhtD Luminex assay has been initially developed and qualified using sera samples from subjects having natural immunity against these 3 proteins. The assay has been evaluated in phase I - II studies and in SPNG005 Cohort 1. During re-qualification with standard based on post- vaccination serum, assay consistency was found to be insufficient. Therefore, the Luminex 3-plex anti-PD, -Ply, -PhtD was replaced by 3 qualified individual ELISAs.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

Anti-Ply haemolysis activity inhibition assay for cohort 2 analysis was no longer available. No analysis was performed for ELISA 6C and OPA-6C as no specific qualified/validated assay was available.
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Notes: