



Clinical trial results:

A phase IIIa open, randomised, controlled study to assess the safety, reactogenicity and immunogenicity induced by a booster dose of GlaxoSmithKline (GSK) Biologicals 10-valent pneumococcal conjugate vaccine when co-administered with GSK Biologicals' measles-mumps-rubella-varicella vaccine (MMRV) vaccine in children during their second year of life, previously vaccinated in infancy in the primary study 10PN-PD-DIT-001 (105553) with GSK Biologicals 10-valent pneumococcal conjugate vaccine.

Summary

EudraCT number	2006-001934-42
Trial protocol	FI
Global end of trial date	21 December 2007

Results information

Result version number	v1 (current)
This version publication date	22 March 2016
First version publication date	29 April 2015

Trial information

Trial identification

Sponsor protocol code	107706
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00370227
WHO universal trial number (UTN)	-

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	31 January 2008
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	21 December 2007
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the incidence of post-immunization rectal fever $>39.0^{\circ}\text{C}$ following a booster dose of GSK Biologicals' 10-valent pneumococcal conjugate vaccine, when co-administered with the first dose of MMRV vaccine in children 12 to 14 months of age.

Protection of trial subjects:

All subjects were supervised after vaccination administration with appropriate medical treatment readily available. Vaccines/products were administered by qualified and trained personnel. Vaccines/products were administered only to eligible subjects that had no contraindications to any components of the vaccines/products. In addition, careful assessment of subjects was performed as regards the following: risk of/ contraindication to further vaccination with DTPa-HBV-IPV/Hib and MMRV vaccines. Concerning the DTPa-HBV-IPV/Hib vaccine, occurrences of encephalopathy within 7 days from vaccination and of fever (rectally) equal or higher than 40.5°C within 48 hours of vaccination were closely followed up. Concerning the MMRV vaccine, since it is recommended that members of the investigational team and subjects' environment be as much as possible immune to varicella, the presence of a susceptible high-risk person (e.g., newborns between 0-4 weeks old, pregnant women with negative history of chickenpox and without recorded vaccination against chickenpox, immunocompromised persons including those with HIV) in the same household as the subject during the study period was considered as an exclusion criteria. It was also recommended that this information be given to the parents/guardians such that, in the advent of a member of the household becoming high-risk within the period of the study, vaccine recipients and especially those who may develop a vaccine-associated rash would avoid close association with these susceptible high-risk individuals. In such circumstances, the potential risk of transmission of the attenuated virus present in the vaccine was to be weighed against the risk of infection and subsequent transmission of natural varicella by individuals who did not benefit from vaccination.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 October 2006
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	4 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Finland: 325
Worldwide total number of subjects	325
EEA total number of subjects	325

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)	325
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study included an Active Phase (Days 0 to 84-112 for 10Pn-MMRV & DTPa-HBV-IPV/Hib-MMRV groups and Days 0 to 42-56 for 10Pn-DTPa-HBV-IPV/Hib Group), & an Extended Safety Follow-Up (ESFU) Phase of up to 4 months duration (til 20-22 months of age [MoA] for 10Pn-MMRV & DTPa-HBV-IPV/Hib-MMRV groups & til 18-20 MoA for 10Pn-DTPa-HBV-IPV/Hib Group).

Pre-assignment

Screening details:

Screening checks included checks on inclusion/exclusion criteria, contraindications/precautions and subjects' medical history. Parent(s)/guardian(s) of subjects signed informed consent forms. Risk impact from fever (rectally) $\geq 38.0^{\circ}\text{C}$ and/or $\geq 40.5^{\circ}\text{C}$ prior to vaccination and for high risk persons for varicella in the same household were evaluated

Period 1

Period 1 title	Overall Study Period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

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

Arm description:

This group consisted of subjects previously vaccinated with the 10Pn-PD-DiT (or 10Pn) vaccine during the 10PN-PD-DIT-001 (105553) study (EudraCT number: 2005-003300-11). In 105553 study, subjects had been primed with 3 doses of 10Pn vaccine at 2, 3 and 4 months of age (injected intramuscularly [IM] in the right thigh) co-administered with DTPa-HBV-IPV/Hib vaccine (or Infanrix hexa™), except for the 2nd dose in France, which was co-administered with DTPa-IPV/Hib (or Infanrix™ IPV Hib), injected IM in the left thigh. In this 107706 study, subjects received at 12 to 14 months of age a booster dose of 10Pn vaccine co-administered with the 1st dose of Priorix-Tetra™ (or MMRV vaccine), and, at 14 to 16 months of age, the 2nd dose of MMRV vaccine co-administered with a booster dose of DTPa-HBV-IPV/Hib vaccine. The 10Pn and DTPa-HBV-IPV/Hib vaccines were administered IM in the left thigh or deltoid and the MMRV vaccine subcutaneously in the right deltoid.

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

Dosage and administration details:

One booster dose administered intramuscularly at 12-14 months of age in the left thigh or deltoid

Investigational medicinal product name	Priorix-Tetra™
Investigational medicinal product code	
Other name	MMRV vaccine; GSK Biologicals' combined measles-mumps-rubella-varicella vaccine
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

2 doses administered subcutaneously in the right deltoid at 12-14 and at 14-16 months of age.

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

Routes of administration	Intramuscular use
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Dosage and administration details:

One dose administered intramuscularly at 14-16 months of age in the left thigh or deltoid.

Arm title	DTPa-HBV-IPV/Hib-MMRV Group
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Arm description:

This group consisted of subjects previously vaccinated with the 10Pn-PD-DiT (or 10Pn) vaccine during the 10PN-PD-DIT-001 (105553) study (EudraCT number: 2005-003300-11). In the 105553 study, subjects had been primed with 3 doses of 10Pn vaccine at 2, 3 and 4 months of age (injected intramuscularly [IM] in the right thigh) co-administered with DTPa-HBV-IPV/Hib vaccine (or Infanrix hexa™), except for the 2nd dose in France, which was co-administered with DTPa-IPV/Hib (or Infanrix™ IPV Hib), injected IM in the left thigh. In this 107706 study, subjects received at 12 to 14 months of age a booster dose of DTPa-HBV-IPV/Hib vaccine co-administered with the 1st dose of Priorix-Tetra™ (or MMRV vaccine), and, at 14 to 16 months of age, the 2nd dose of MMRV vaccine co-administered with a booster dose of 10Pn vaccine. The 10Pn and DTPa-HBV-IPV/Hib vaccines were administered IM in the left thigh or deltoid and the MMRV vaccine subcutaneously in the right deltoid.

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

Dosage and administration details:

One booster dose administered at 14-16 months of age in the left thigh or deltoid

Investigational medicinal product name	Priorix-Tetra™
Investigational medicinal product code	
Other name	MMRV vaccine; GSK Biologicals' combined measles-mumps-rubella-varicella vaccine
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

2 doses administered subcutaneously in the right deltoid at 12-14 and at 14-16 months of age.

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

Dosage and administration details:

One dose administered intramuscularly at 12-14 months of age in the left thigh or deltoid.

Arm title	10Pn-DTPa-HBV-IPV/Hib Group
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Arm description:

This group consisted of subjects previously vaccinated with the 10Pn-PD-DiT (or 10Pn) vaccine during the 10PN-PD-DIT-001 (105553) study (EudraCT number: 2005-003300-11). In the 105553 study, subjects had been primed with 3 doses of 10Pn vaccine at 2, 3 and 4 months of age (injected intramuscularly [IM] in the right thigh) co-administered with DTPa-HBV-IPV/Hib vaccine (or Infanrix hexa™), except for the second dose in France, which was co-administered with DTPa-IPV/Hib (or Infanrix™ IPV Hib), injected IM in the left thigh. In this 107706 study, subjects received at 12 to 14 months of age a booster dose of 10Pn vaccine co-administered with a booster dose of DTPa-HBV-IPV/Hib vaccine. The 10Pn and DTPa-HBV-IPV/Hib vaccines were administered IM in the thigh or deltoid, respectively in the left and right side.

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

Dosage and administration details:

One booster dose administered at 14-16 months of age in the left thigh or deltoid

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

Dosage and administration details:

One dose administered intramuscularly at 12-14 months of age in the right thigh or deltoid.

Number of subjects in period 1	10Pn-MMRV Group	DTPa-HBV-IPV/Hib-MMRV Group	10Pn-DTPa-HBV-IPV/Hib Group
Started	110	101	114
Completed	108	100	111
Not completed	2	1	3
Consent withdrawn by subject	1	1	2
Lost to follow-up	1	-	1

Baseline characteristics

Reporting groups

Reporting group title	10Pn-MMRV Group
Reporting group description:	
This group consisted of subjects previously vaccinated with the 10Pn-PD-DiT (or 10Pn) vaccine during the 10PN-PD-DIT-001 (105553) study (EudraCT number: 2005-003300-11). In 105553 study, subjects had been primed with 3 doses of 10Pn vaccine at 2, 3 and 4 months of age (injected intramuscularly [IM] in the right thigh) co-administered with DTPa-HBV-IPV/Hib vaccine (or Infanrix hexa™), except for the 2nd dose in France, which was co-administered with DTPa-IPV/Hib (or Infanrix™ IPV Hib), injected IM in the left thigh. In this 107706 study, subjects received at 12 to 14 months of age a booster dose of 10Pn vaccine co-administered with the 1st dose of Priorix-Tetra™ (or MMRV vaccine), and, at 14 to 16 months of age, the 2nd dose of MMRV vaccine co-administered with a booster dose of DTPa-HBV-IPV/Hib vaccine. The 10Pn and DTPa-HBV-IPV/Hib vaccines were administered IM in the left thigh or deltoid and the MMRV vaccine subcutaneously in the right deltoid.	
Reporting group title	DTPa-HBV-IPV/Hib-MMRV Group
Reporting group description:	
This group consisted of subjects previously vaccinated with the 10Pn-PD-DiT (or 10Pn) vaccine during the 10PN-PD-DIT-001 (105553) study (EudraCT number: 2005-003300-11). In the 105553 study, subjects had been primed with 3 doses of 10Pn vaccine at 2, 3 and 4 months of age (injected intramuscularly [IM] in the right thigh) co-administered with DTPa-HBV-IPV/Hib vaccine (or Infanrix hexa™), except for the 2nd dose in France, which was co-administered with DTPa-IPV/Hib (or Infanrix™ IPV Hib), injected IM in the left thigh. In this 107706 study, subjects received at 12 to 14 months of age a booster dose of DTPa-HBV-IPV/Hib vaccine co-administered with the 1st dose of Priorix-Tetra™ (or MMRV vaccine), and, at 14 to 16 months of age, the 2nd dose of MMRV vaccine co-administered with a booster dose of 10Pn vaccine. The 10Pn and DTPa-HBV-IPV/Hib vaccines were administered IM in the left thigh or deltoid and the MMRV vaccine subcutaneously in the right deltoid.	
Reporting group title	10Pn-DTPa-HBV-IPV/Hib Group
Reporting group description:	
This group consisted of subjects previously vaccinated with the 10Pn-PD-DiT (or 10Pn) vaccine during the 10PN-PD-DIT-001 (105553) study (EudraCT number: 2005-003300-11). In the 105553 study, subjects had been primed with 3 doses of 10Pn vaccine at 2, 3 and 4 months of age (injected intramuscularly [IM] in the right thigh) co-administered with DTPa-HBV-IPV/Hib vaccine (or Infanrix hexa™), except for the second dose in France, which was co-administered with DTPa-IPV/Hib (or Infanrix™ IPV Hib), injected IM in the left thigh. In this 107706 study, subjects received at 12 to 14 months of age a booster dose of 10Pn vaccine co-administered with a booster dose of DTPa-HBV-IPV/Hib vaccine. The 10Pn and DTPa-HBV-IPV/Hib vaccines were administered IM in the thigh or deltoid, respectively in the left and right side.	

Reporting group values	10Pn-MMRV Group	DTPa-HBV-IPV/Hib-MMRV Group	10Pn-DTPa-HBV-IPV/Hib Group
Number of subjects	110	101	114
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			

Age continuous Units: months arithmetic mean standard deviation	12.3 ± 0.48	12.3 ± 0.5	12.3 ± 0.52
Gender categorical Units: Subjects			
Female	49	52	65
Male	61	49	49

Reporting group values	Total		
Number of subjects	325		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Age continuous Units: months arithmetic mean standard deviation	-		
Gender categorical Units: Subjects			
Female	166		
Male	159		

End points

End points reporting groups

Reporting group title	10Pn-MMRV Group
Reporting group description:	
This group consisted of subjects previously vaccinated with the 10Pn-PD-DiT (or 10Pn) vaccine during the 10PN-PD-DIT-001 (105553) study (EudraCT number: 2005-003300-11). In 105553 study, subjects had been primed with 3 doses of 10Pn vaccine at 2, 3 and 4 months of age (injected intramuscularly [IM] in the right thigh) co-administered with DTPa-HBV-IPV/Hib vaccine (or Infanrix hexa™), except for the 2nd dose in France, which was co-administered with DTPa-IPV/Hib (or Infanrix™ IPV Hib), injected IM in the left thigh. In this 107706 study, subjects received at 12 to 14 months of age a booster dose of 10Pn vaccine co-administered with the 1st dose of Priorix-Tetra™ (or MMRV vaccine), and, at 14 to 16 months of age, the 2nd dose of MMRV vaccine co-administered with a booster dose of DTPa-HBV-IPV/Hib vaccine. The 10Pn and DTPa-HBV-IPV/Hib vaccines were administered IM in the left thigh or deltoid and the MMRV vaccine subcutaneously in the right deltoid.	
Reporting group title	DTPa-HBV-IPV/Hib-MMRV Group
Reporting group description:	
This group consisted of subjects previously vaccinated with the 10Pn-PD-DiT (or 10Pn) vaccine during the 10PN-PD-DIT-001 (105553) study (EudraCT number: 2005-003300-11). In the 105553 study, subjects had been primed with 3 doses of 10Pn vaccine at 2, 3 and 4 months of age (injected intramuscularly [IM] in the right thigh) co-administered with DTPa-HBV-IPV/Hib vaccine (or Infanrix hexa™), except for the 2nd dose in France, which was co-administered with DTPa-IPV/Hib (or Infanrix™ IPV Hib), injected IM in the left thigh. In this 107706 study, subjects received at 12 to 14 months of age a booster dose of DTPa-HBV-IPV/Hib vaccine co-administered with the 1st dose of Priorix-Tetra™ (or MMRV vaccine), and, at 14 to 16 months of age, the 2nd dose of MMRV vaccine co-administered with a booster dose of 10Pn vaccine. The 10Pn and DTPa-HBV-IPV/Hib vaccines were administered IM in the left thigh or deltoid and the MMRV vaccine subcutaneously in the right deltoid.	
Reporting group title	10Pn-DTPa-HBV-IPV/Hib Group
Reporting group description:	
This group consisted of subjects previously vaccinated with the 10Pn-PD-DiT (or 10Pn) vaccine during the 10PN-PD-DIT-001 (105553) study (EudraCT number: 2005-003300-11). In the 105553 study, subjects had been primed with 3 doses of 10Pn vaccine at 2, 3 and 4 months of age (injected intramuscularly [IM] in the right thigh) co-administered with DTPa-HBV-IPV/Hib vaccine (or Infanrix hexa™), except for the second dose in France, which was co-administered with DTPa-IPV/Hib (or Infanrix™ IPV Hib), injected IM in the left thigh. In this 107706 study, subjects received at 12 to 14 months of age a booster dose of 10Pn vaccine co-administered with a booster dose of DTPa-HBV-IPV/Hib vaccine. The 10Pn and DTPa-HBV-IPV/Hib vaccines were administered IM in the thigh or deltoid, respectively in the left and right side.	

Primary: Number of subjects with fever as solicited general symptom

End point title	Number of subjects with fever as solicited general symptom ^[1]
End point description:	
Fever as solicited general symptom was defined as rectal temperature above 39.0 degrees centigrade (°C).	
End point type	Primary
End point timeframe:	
Within 15 days (Day 0-14) post vaccination with Dose 1 (D1) (= booster dose of 10Pn and the first dose of MMRV vaccine)	
Notes:	
[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.	
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.	

End point values	10Pn-MMRV Group	DTPa-HBV-IPV/Hib-MMRV Group	10Pn-DTPa-HBV-IPV/Hib Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	109	101	112	
Units: Subjects				
Fever (>39.0°C), post D1 (N=109;101;112)	31	33	9	

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of subjects with any and grade 3 solicited local symptoms
End point description:	
Solicited local symptoms assessed were pain, redness and swelling at the injection site (in MedDRA terms: injection site pain, redness and swelling). Grade 3 pain was defined as crying when limb was moved/spontaneously painful. Grade 3 swelling/redness was defined as swelling/redness larger than (>) 30 millimeters (mm). "Any" is defined as incidence of the specified symptom regardless of intensity.	
End point type	Secondary
End point timeframe:	
Within 4 days (Days 0-3) post vaccination, across doses	

End point values	10Pn-MMRV Group	DTPa-HBV-IPV/Hib-MMRV Group	10Pn-DTPa-HBV-IPV/Hib Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	109	101	112	
Units: Subjects				
Any Pain, Across doses (N=109;101;112)	69	50	73	
Grade 3 Pain, Across doses (N=109;101;112)	6	0	4	
Any Redness, Across doses (N=109;101;112)	79	75	70	
Grade 3 Redness, Across doses (N=109;101;112)	13	7	7	
Any Swelling, Across doses (N=109;101;112)	58	57	52	
Grade 3 Swelling, Across doses (N=109;101;112)	16	9	6	

Statistical analyses

No statistical analyses for this end point

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

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

Solicited general symptoms assessed were drowsiness (Drows), irritability (Irr) and loss of appetite (Loss App). Grade 3 (G3) Drows was defined as drowsiness that prevented normal activity. G3 Irr was defined as crying that could not be comforted/which prevented normal activity. G3 Loss App was defined as not eating at all. Any was defined as incidence of the specified symptom regardless of intensity/relationship to vaccination.

End point type	Secondary
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End point timeframe:

Within 4 days (Days 0-3) post vaccination, across doses

End point values	10Pn-MMRV Group	DTPa-HBV-IPV/Hib-MMRV Group	10Pn-DTPa-HBV-IPV/Hib Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	109	101	112	
Units: Subjects				
Any Drows, Across doses (N=109;101;112)	55	54	57	
G3 Drows, Across doses (N=109;101;112)	0	0	0	
Any Irr, Across doses (N=109;101;112)	80	73	84	
G3 Irr, Across doses (N=109;101;112)	4	1	5	
Any Loss App, Across doses (N=109;101;112)	47	33	37	
G3 Loss App, Across doses (N=109;101;112)	0	0	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any and Grade 3 solicited general symptoms specific to MMRV vaccination

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

Solicited general symptoms assessed were fever (as solicited general symptom following MMRV vaccination defined as rectal temperature higher than or equal to $[\geq]$ 38.0 degrees centigrade [$^{\circ}\text{C}$]), rash (or exanthema) (referred to as 'rash' below), parotid/ salivary gland swelling (referred to as 'parotid gland' below), and any suspected signs of meningism including febrile convulsions (referred to as 'meningism' below). G3 fever was defined as rectal temperature higher than ($>$) 40.0 $^{\circ}\text{C}$, G3 meningism as meningism which prevented normal, everyday activity, G3 parotid gland as swelling with accompanying symptoms and G3 rash as subject presenting \geq 150 lesions. Any was defined as incidence of the specified symptom regardless of intensity/relationship to vaccination.

End point type	Secondary
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End point timeframe:

Within 43 days (Days 0-42) post vaccination, across doses

End point values	10Pn-MMRV Group	DTPa-HBV-IPV/Hib-MMRV Group	10Pn-DTPa-HBV-IPV/Hib Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	109	101	112	
Units: Subjects				
Any Fever ($\geq 38.0^{\circ}\text{C}$), across doses (N=109;101;112)	101	88	69	
G3 Fever ($> 40.0^{\circ}\text{C}$), across doses (N=109;101;112)	6	6	4	
Any Meningism, across doses (N=109;101;112)	0	0	1	
G3 Meningism, across doses (N=109;101;112)	0	0	1	
Any Parotid Gland, across doses (N=109;101;112)	0	0	0	
G3 Parotid Gland, across doses (N=109;101;112)	0	0	0	
Any Rash, across doses (N=109;101;112)	38	48	18	
G3 Rash, across doses (N=109;101;112)	8	11	2	

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of subjects with unsolicited adverse events (AEs)
End point description:	
An AE is any untoward medical occurrence in a clinical investigation subject, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. "Any" is defined an incidence of an unsolicited AE regardless of intensity or relationship to study vaccination.	
End point type	Secondary
End point timeframe:	
Within 43 days (Days 0-42) post vaccination, across doses	

End point values	10Pn-MMRV Group	DTPa-HBV-IPV/Hib-MMRV Group	10Pn-DTPa-HBV-IPV/Hib Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	110	101	114	
Units: Subjects				
Any unsolicited AEs	88	80	78	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with serious adverse events (SAEs) during the Active Phase of the study, for subjects in 10Pn-MMRV and DTPa-HBV-IPV/Hib-MMRV groups

End point title	Number of subjects with serious adverse events (SAEs) during the Active Phase of the study, for subjects in 10Pn-MMRV and DTPa-HBV-IPV/Hib-MMRV groups ^[2]
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End point description:

An SAE is any untoward medical occurrence that: results in death, is life-threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, or may evolve into one of the outcomes listed above. Any is defined an incidence of a SAE regardless of intensity/severity . The endpoint only concerns subjects in 10Pn-MMRV and DTPa-HBV-IPV/Hib-MMRV groups, for whom the Active Phase of the study ended at Day 86-112.

End point type	Secondary
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End point timeframe:

From Day 0 to Day 86-112 (from 12-14 to 16-18 months of age for subjects)

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This endpoint was only analysed in the 10Pn-MMRV and DTPa-HBV-IPV/Hib-MMRV groups.

End point values	10Pn-MMRV Group	DTPa-HBV-IPV/Hib-MMRV Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	110	101		
Units: Subjects				
Any SAE(s)	2	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with serious adverse events (SAEs) during the Active Phase of the study, for subjects in 10Pn-DTPa-HBV-IPV/Hib Group

End point title	Number of subjects with serious adverse events (SAEs) during the Active Phase of the study, for subjects in 10Pn-DTPa-HBV-IPV/Hib Group ^[3]
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End point description:

An SAE is any untoward medical occurrence that: results in death, is life-threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, or may evolve into one of the outcomes listed above. Any is defined an incidence of a SAE regardless of intensity/severity . The endpoint only concerns subjects in 10Pn-DTPa-HBV-IPV/Hib Group, for whom the Active Phase of the study ended at Day 42-56.

End point type	Secondary
End point timeframe:	
From Day 0 to Day 42-56 (from 12-14 to 14-16 months of age for subjects)	
Notes:	
[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.	
Justification: This endpoint was only analysed in the 10Pn-DTPa-HBV-IPV/Hib Group	

End point values	10Pn-DTPa-HBV-IPV/Hib Group			
Subject group type	Reporting group			
Number of subjects analysed	114			
Units: Subjects				
Any SAE(s)	1			

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of subjects with serious adverse events (SAEs) throughout the entire study
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End point description:

An SAE is any untoward medical occurrence that: results in death, is life-threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, or may evolve into one of the outcomes listed above. Any is defined an incidence of a SAE regardless of intensity/severity . Please note that this endpoint was analysed only in subjects participating to the ESFU Phase (that is, 108, 100 and 111 subjects in the 10Pn-MMRV, DTPa-HBV-IPV/Hib-MMRV and 10Pn-DTPa-HBV-IPV/Hib Groups, respectively).

End point type	Secondary
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End point timeframe:

Throughout the entire study, e. a. during the Active and ESFU phases of the study (from Day 0 to Day 222-266 for 10Pn-MMRV and DTPa-HBV-IPV/Hib-MMRV groups, and to Day 180-210 for 10Pn-DTPa-HBV-IPV/Hib Group)

End point values	10Pn-MMRV Group	DTPa-HBV-IPV/Hib-MMRV Group	10Pn-DTPa-HBV-IPV/Hib Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	108	100	111	
Units: Subjects				
Any SAE(s)	5	3	4	

Statistical analyses

Secondary: Number of subjects with seroprotective levels of antibodies against anti-pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F antigens

End point title	Number of subjects with seroprotective levels of antibodies against anti-pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F antigens ^[4]
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End point description:

A subject with seroprotective levels of antibodies against pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F antigens was defined as a subject with anti-pneumococcal serotype antibody concentration above than or equal to (\geq) 0.20 microgram per millilitre ($\mu\text{g/mL}$). Anti-pneumococcal serotypes antibodies assessed were antibodies against pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F (Anti-1, -4, -5, -6B, -7F, 9V, -14, -18C, -19F and -23F). Analysis was performed using the 22F-inhibition Enzyme-linked immunosorbent assay (ELISA), using $\geq 0.05 \mu\text{g/mL}$ as seropositivity cut off. This endpoint was assessed solely in the 10Pn-MMRV and 10Pn-DTPa-HBV-IPV/Hib groups.

End point type	Secondary
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End point timeframe:

Prior to (PRE) and Day 42 (Day 42-56 after booster vaccination with 10Pn/1st Dose MMRV)

Notes:

[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: This endpoint was only analysed in the 10Pn-MMRV and 10Pn-DTPa-HBV-IPV/Hib groups.

End point values	10Pn-MMRV Group	10Pn-DTPa-HBV-IPV/Hib Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	108	110		
Units: Subjects				
Anti-1 , PRE (N=107;110)	47	62		
Anti-1 , Day 42 (N=104;106)	103	104		
Anti-4 , PRE (N=106;110)	74	88		
Anti-4 , Day 42 (N=104;106)	104	106		
Anti-5 , PRE (N=106;110)	81	95		
Anti-5 , Day 42 (N=104;106)	104	105		
Anti-6B , PRE (N=106;110)	77	86		
Anti-6B , Day 42 (N=104;106)	100	99		
Anti-7F , PRE (N=108;110)	103	107		
Anti-7F , Day 42 (N=104;106)	104	106		
Anti-9V , PRE (N=106;110)	101	104		
Anti-9V , Day 42 (N=104;106)	104	105		
Anti-14 , PRE (N=107;110)	102	105		
Anti-14 , Day 42 (N=104;106)	103	106		
Anti-18C , PRE (N=107;110)	81	97		
Anti-18C , Day 42 (N=104;106)	104	106		
Anti-19F , PRE (N=106;110)	87	95		
Anti-19F , Day 42 (N=104;106)	101	104		
Anti-23F , PRE (N=106;110)	68	88		
Anti-23F , Day 42 (N=104;106)	101	100		

Statistical analyses

Secondary: Antibody concentrations against pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F (Anti-1, -4, -5, -6B, -7F, 9V, -14, -18C, -19F and -23F).

End point title	Antibody concentrations against pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F (Anti-1, -4, -5, -6B, -7F, 9V, -14, -18C, -19F and -23F). ^[5]
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End point description:

Anti-pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F antibody concentrations (Anti-1, -4, -5, -6B, -7F, -9V, -14, -18C, -19F and -23F) were calculated, expressed as geometric mean concentrations (GMCs), in microgram per millilitre (µg/mL). The seropositivity cut-off for the assay was ≥ 0.05 µg/mL. Antibody concentrations < 0.05 µg/mL were given an arbitrary value of half the cut-off for the purpose of GMC calculation. This endpoint was assessed solely in the 10Pn-MMRV and 10Pn-DTPa-HBV-IPV/Hib groups.

End point type	Secondary
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End point timeframe:

Prior to (PRE) and Day 42 (Day 42-56 after booster vaccination with 10Pn/1st Dose MMRV)

Notes:

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

Justification: This endpoint was only analysed in the 10Pn-MMRV and 10Pn-DTPa-HBV-IPV/Hib groups.

End point values	10Pn-MMRV Group	10Pn-DTPa-HBV-IPV/Hib Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	108	110		
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-1 , PRE (N=107;110)	0.17 (0.15 to 0.21)	0.21 (0.18 to 0.25)		
Anti-1 , Day 42 (N=104;106)	1.11 (0.96 to 1.28)	1.15 (0.98 to 1.34)		
Anti-4 , PRE (N=106;110)	0.33 (0.27 to 0.39)	0.43 (0.36 to 0.51)		
Anti-4 , Day 42 (N=104;106)	2.11 (1.83 to 2.42)	1.98 (1.72 to 2.27)		
Anti-5 , PRE (N=106;110)	0.33 (0.28 to 0.39)	0.33 (0.28 to 0.39)		
Anti-5 , Day 42 (N=104;106)	1.61 (1.36 to 1.89)	1.61 (1.36 to 1.89)		
Anti-6B , PRE (N=106;110)	0.33 (0.27 to 0.41)	0.37 (0.3 to 0.45)		
Anti-6B , Day 42 (N=104;106)	1.42 (1.17 to 1.73)	1.34 (1.07 to 1.69)		
Anti-7F , PRE (N=108;110)	0.77 (0.66 to 0.89)	0.94 (0.82 to 1.08)		
Anti-7F , Day 42 (N=104;106)	2.94 (2.62 to 3.3)	3.43 (3.04 to 3.87)		
Anti-9V , PRE (N=106;110)	0.64 (0.56 to 0.74)	0.8 (0.68 to 0.94)		
Anti-9V , Day 42 (N=104;106)	2.33 (2.05 to 2.65)	2.56 (2.25 to 2.92)		
Anti-14 , PRE (N=107;110)	1.13 (0.93 to 1.37)	1.27 (1.05 to 1.54)		
Anti-14 , Day 42 (N=104;106)	4.18 (3.53 to 4.97)	4.32 (3.73 to 5.01)		
Anti-18C , PRE (N=107;110)	0.38 (0.32 to 0.45)	0.54 (0.45 to 0.64)		

Anti-18C , Day 42 (N=104;106)	4.14 (3.66 to 4.68)	3.99 (3.53 to 4.52)		
Anti-19F , PRE (N=106;110)	0.53 (0.42 to 0.66)	0.7 (0.56 to 0.87)		
Anti-19F , Day 42 (N=104;106)	4.23 (3.4 to 5.27)	3.62 (3.03 to 4.32)		
Anti-23F , PRE (N=106;110)	0.34 (0.27 to 0.43)	0.46 (0.36 to 0.6)		
Anti-23F , Day 42 (N=104;106)	1.68 (1.36 to 2.08)	1.65 (1.34 to 2.04)		

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations to protein D

End point title	Antibody concentrations to protein D ^[6]
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End point description:

Anti-protein D (Anti-PD) antibody concentrations by Enzyme-Linked Immunosorbent Assay (ELISA) were calculated, expressed as geometric mean concentrations (GMCs) in ELISA unit per milli-liter (EL.U/mL) and tabulated. The seropositivity cut-off for the assay was ≥ 100 EL.U/mL. Antibody concentrations < 100 EL.U/mL were given an arbitrary value of half the cut-off for the purpose of GMC calculation. This endpoint was assessed solely in the 10Pn-MMRV and 10Pn-DTPa-HBV-IPV/Hib groups.

End point type	Secondary
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End point timeframe:

Prior to (PRE) and Day 42 (Day 42-56 after booster vaccination with 10Pn/1st Dose MMRV)

Notes:

[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: This endpoint was only analysed in the 10Pn-MMRV and 10Pn-DTPa-HBV-IPV/Hib groups.

End point values	10Pn-MMRV Group	10Pn-DTPa-HBV-IPV/Hib Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	108	108		
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PD, PRE (N= 108;108)	594.8 (490.7 to 720.8)	717.6 (582 to 884.7)		
Anti-PD, Day 42 (N=104;106)	2655.8 (2123.9 to 3320.8)	2666 (2190.1 to 3245.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with seroprotective levels of antibodies against pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F antigens

End point title	Number of subjects with seroprotective levels of antibodies
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End point description:

A subject with seroprotective levels of antibodies against pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F antigens was defined as a subject with anti-pneumococcal serotype antibody concentration above than or equal to (\geq) 0.20 microgram per millilitre ($\mu\text{g/mL}$). Anti-pneumococcal serotypes antibodies assessed were antibodies against pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F (Anti-1, -4, -5, -6B, -7F, 9V, -14, -18C, -19F and -23F). Analysis was performed using the 22F-inhibition Enzyme-linked immunosorbent assay (ELISA), using $\geq 0.05 \mu\text{g/mL}$ as seropositivity cut off. This endpoint was assessed solely in the DTPa-HBV-IPV/Hib-MMRV Group.

End point type	Secondary
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End point timeframe:

Prior to (PRE) and Day 84 (Day 42-56 after 2nd dose MMRV)

Notes:

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

Justification: This endpoint was only analysed in the DTPa-HBV-IPV/Hib-MMRV Group

End point values	DTPa-HBV-IPV/Hib-MMRV Group			
Subject group type	Reporting group			
Number of subjects analysed	93			
Units: Subjects				
Anti-1 , PRE (N=92)	45			
Anti-1 , Day 84 (N=91)	88			
Anti-4 , PRE (N=92)	72			
Anti-4 , Day 84 (N=91)	91			
Anti-5 , PRE (N=92)	78			
Anti-5 , Day 84 (N=91)	91			
Anti-6B , PRE (N=92)	81			
Anti-6B , Day 84 (N=91)	87			
Anti-7F , PRE (N=91)	89			
Anti-7F , Day 84 (N=91)	91			
Anti-9V , PRE (N=92)	83			
Anti-9V , Day 84 (N=91)	91			
Anti-14 , PRE (N=92)	85			
Anti-14 , Day 84 (N=91)	91			
Anti-18C , PRE (N=93)	77			
Anti-18C , Day 84 (N=91)	90			
Anti-19F , PRE (N=93)	81			
Anti-19F , Day 84 (N=91)	91			
Anti-23F , PRE (N=92)	72			
Anti-23F , Day 84 (N=91)	90			

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations against pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F (Anti-1, -4, -5, -6B, -7F, 9V, -14, -18C, -19F and -23F).

End point title	Antibody concentrations against pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F (Anti-1, -4, -5, -6B, -7F,
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End point description:

Anti-pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F antibody concentrations (Anti-1, -4, -5, -6B, -7F, -9V, -14, -18C, -19F and -23F) were calculated, expressed as geometric mean concentrations (GMCs), in microgram per millilitre ($\mu\text{g/mL}$). The seropositivity cut-off for the assay was $\geq 0.05 \mu\text{g/mL}$. Antibody concentrations $< 0.05 \mu\text{g/mL}$ were given an arbitrary value of half the cut-off for the purpose of GMC calculation. This endpoint was assessed solely in the DTPa-HBV-IPV/Hib-MMRV Group.

End point type	Secondary
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End point timeframe:

Prior to (PRE) and Day 84 (Day 84-56 after 2nd dose MMRV)

Notes:

[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: This endpoint was only analysed in the DTPa-HBV-IPV/Hib-MMRV Group.

End point values	DTPa-HBV-IPV/Hib-MMRV Group			
Subject group type	Reporting group			
Number of subjects analysed	93			
Units: $\mu\text{g/mL}$				
geometric mean (confidence interval 95%)				
Anti-1 , PRE (N=92)	0.19 (0.16 to 0.24)			
Anti-1 , Day 84 (N=91)	1.24 (1.04 to 1.49)			
Anti-4 , PRE (N=92)	0.47 (0.38 to 0.59)			
Anti-4 , Day 84 (N=91)	2.54 (2.16 to 2.98)			
Anti-5 , PRE (N=92)	0.45 (0.38 to 0.53)			
Anti-5 , Day 84 (N=91)	1.93 (1.61 to 2.32)			
Anti-6B , PRE (N=92)	0.51 (0.4 to 0.65)			
Anti-6B , Day 84 (N=91)	1.63 (1.31 to 2.01)			
Anti-7F , PRE (N=91)	0.83 (0.71 to 0.98)			
Anti-7F , Day 84 (N=91)	2.93 (2.55 to 3.36)			
Anti-9V , PRE (N=92)	0.72 (0.59 to 0.87)			
Anti-9V , Day 84 (N=91)	2.6 (2.21 to 3.06)			
Anti-14 , PRE (N=92)	1.21 (0.93 to 1.57)			
Anti-14 , Day 84 (N=91)	4.19 (3.5 to 5.01)			
Anti-18C , PRE (N=93)	0.46 (0.38 to 0.56)			
Anti-18C , Day 84 (N=91)	2.74 (2.3 to 3.26)			
Anti-19F , PRE (N=93)	0.68 (0.54 to 0.86)			
Anti-19F , Day 84 (N=91)	3.94 (3.33 to 4.67)			

Anti-23F , PRE (N=92)	0.47 (0.38 to 0.58)			
Anti-23F , Day 84 (N=91)	2.41 (2.03 to 2.85)			

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations to protein D

End point title	Antibody concentrations to protein D ^[9]
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End point description:

Anti-protein D (Anti-PD) antibody concentrations by Enzyme-Linked Immunosorbent Assay (ELISA) were calculated, expressed as geometric mean concentrations (GMCs) in ELISA unit per milli-liter (EL.U/mL) and tabulated. The seropositivity cut-off for the assay was ≥ 100 EL.U/mL. Antibody concentrations < 100 EL.U/mL were given an arbitrary value of half the cut-off for the purpose of GMC calculation. This endpoint was assessed solely in the DTPa-HBV-IPV/Hib-MMRV Group

End point type	Secondary
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End point timeframe:

Prior to (PRE) and Day 84 (Day 84-56 after 2nd dose MMRV)

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: This endpoint was only analysed in the 10Pn-DTPa-HBV-IPV/Hib Group

End point values	DTPa-HBV-IPV/Hib-MMRV Group			
Subject group type	Reporting group			
Number of subjects analysed	91			
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PD, PRE	690.2 (545.2 to 873.7)			
Anti-PD, Day 84	3346.1 (2580.8 to 4338.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with seropositive levels of antibodies against mumps antigens

End point title	Number of subjects with seropositive levels of antibodies against mumps antigens ^[10]
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End point description:

A subject with seropositive levels of antibodies against mumps antigens (S+ Mumps) was defined as a subject with anti-mumps antibody concentrations ≥ 231 units per millilitre (U/mL).

End point type	Secondary
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End point timeframe:

At Day 42 (42-56 days post 1st dose of MMRV vaccine) at Day 84 (42-56 days post 2nd dose of MMRV vaccine)

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: This endpoint was only analysed in the 10Pn-MMRV and DTPa-HBV-IPV/Hib-MMRV groups.

End point values	10Pn-MMRV Group	DTPa-HBV-IPV/Hib-MMRV Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	102	88		
Units: Subjects				
S+ Mumps, Day 42 (N=102;88)	92	79		
S+ Mumps, Day 84 (N=102;89)	99	89		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with seropositive levels of antibodies against rubella antigens

End point title	Number of subjects with seropositive levels of antibodies against rubella antigens ^[11]
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End point description:

A subject with seropositive levels of antibodies against rubella antigens (S+ Rubella) was defined as a subject with anti-rubella antibody concentrations ≥ 4 international units per millilitre (IU/mL).

End point type	Secondary
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End point timeframe:

At Day 42 (42-56 days post 1st dose of MMRV vaccine) at Day 84 (42-56 days post 2nd dose of MMRV vaccine)

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: This endpoint was only analysed in the 10Pn-MMRV and DTPa-HBV-IPV/Hib-MMRV groups.

End point values	10Pn-MMRV Group	DTPa-HBV-IPV/Hib-MMRV Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	102	89		
Units: Subjects				
S+ Rubella, Day 42 (N=102;88)	102	86		
S+ Rubella, Day 84 (N=102;89)	101	89		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with seropositive levels of antibodies against varicella antigens

End point title	Number of subjects with seropositive levels of antibodies against varicella antigens ^[12]
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End point description:

A subject with seropositive levels of antibodies against varicella antigens (S+ Varicella) was defined as a subject with anti-varicella antibody titers ≥ 4 .

End point type	Secondary
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End point timeframe:

At Day 42 (42-56 days post 1st dose of MMRV vaccine) at Day 84 (42-56 days post 2nd dose of MMRV vaccine)

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: This endpoint was only analysed in the 10Pn-MMRV and DTPa-HBV-IPV/Hib-MMRV groups.

End point values	10Pn-MMRV Group	DTPa-HBV-IPV/Hib-MMRV Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	100	89		
Units: Subjects				
S+ Varicella, Day 42 (N=99;87)	99	85		
S+ Varicella, Day 84 (N=100;89)	100	89		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seroconverted as regards antibodies against measles antigens

End point title	Number of subjects seroconverted as regards antibodies against measles antigens ^[13]
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End point description:

Seroconversion for measles (SCR Measles) was defined as a) appearance of antibody levels \geq the 150 milli-International units per millilitre (mIU/mL) seropositivity assay cut-off in seronegative subjects prior to dose 1 of MMRV vaccine or b) Appearance of antibody levels \geq the 150 mIU/mL seropositivity assay cut-off in seronegative subjects prior to Dose 1 and 42-56 days after the first dose of MMRV vaccine (prior to Dose 2 of MMRV vaccine). Only the appearance of antibody levels \geq the 150 mIU/mL seropositivity assay cut-off as assessed at 42-56 days after the second dose of MMRV vaccine, and in seronegative subjects prior to Dose 1 was analysed and tabulated. A seronegative subject as regards antibodies against measles antigens was defined as a subject with anti-measles antibody concentrations < 150 mIU/mL.

End point type	Secondary
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End point timeframe:

At Day 42 (42-56 days post 1st dose of MMRV vaccine) at Day 84 (42-56 days post 2nd dose of MMRV vaccine)

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: This endpoint was only analysed in the 10Pn-MMRV and DTPa-HBV-IPV/Hib-MMRV groups.

End point values	10Pn-MMRV Group	DTPa-HBV-IPV/Hib-MMRV Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	102	89		
Units: Subjects				
SCR Measles, Day 42 (N=102;88)	100	86		
SCR Measles, Day 84 (N=102;89)	101	89		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seroconverted as regards antibodies against mumps antigens

End point title	Number of subjects seroconverted as regards antibodies against mumps antigens ^[14]
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End point description:

Seroconversion for mumps (SCR Mumps) was defined as a) appearance of antibody levels \geq the 231 units per millilitre (U/mL) seropositivity assay cut-off of in seronegative subjects prior to dose 1 of MMRV vaccine or b) appearance of antibody levels \geq the 231 U/mL seropositivity assay cut-off in seronegative subjects prior to Dose 1 and 42-56 days after the first dose of MMRV vaccine (prior to Dose 2 of MMRV vaccine). Only the appearance of antibody levels \geq the 231 U/mL seropositivity assay cut-off as assessed at 42-56 days after the second dose of MMRV vaccine, and in seronegative subjects prior to Dose 1 was analysed and tabulated.

A subject with seronegative levels of antibodies against mumps antigens was defined as a subject with anti-mumps antibody concentrations $<$ 231 units per millilitre (U/mL).

End point type	Secondary
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End point timeframe:

At Day 42 (42-56 days post 1st dose of MMRV vaccine) at Day 84 (42-56 days post 2nd dose of MMRV vaccine)

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: This endpoint was only analysed in the 10Pn-MMRV and DTPa-HBV-IPV/Hib-MMRV groups.

End point values	10Pn-MMRV Group	DTPa-HBV-IPV/Hib-MMRV Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	102	89		
Units: Subjects				
SCR Mumps, Day 42 (N=102;88)	92	88		
SCR Mumps, Day 84 (N=102;89)	99	89		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seroconverted as regards antibodies against rubella

antigens

End point title	Number of subjects seroconverted as regards antibodies against rubella antigens ^[15]
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End point description:

Seroconversion for rubella (SCR Rubella) was defined as a) appearance of antibody levels \geq the 4 international units per millilitre (IU/mL) seropositivity assay cut-off in seronegative subjects prior to dose 1 of MMRV vaccine or b) appearance of antibody levels \geq the 4 IU/mL seropositivity assay cut-off in seronegative subjects prior to Dose 1 and 42-56 days after the first dose of MMRV vaccine (prior to Dose 2 of MMRV vaccine). Only the appearance of antibody levels \geq the 4 IU/mL seropositivity assay cut-off as assessed at 42-56 days after the second dose of MMRV vaccine, and in seronegative subjects prior to Dose 1 was analysed and tabulated.

A subject with seronegative levels of antibodies against rubella antigens was defined as a subject with anti-rubella antibody concentrations < 4 IU/mL.

End point type	Secondary
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End point timeframe:

At Day 42 (42-56 days post 1st dose of MMRV vaccine) at Day 84 (42-56 days post 2nd dose of MMRV vaccine)

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: This endpoint was only analysed in the 10Pn-MMRV and DTPa-HBV-IPV/Hib-MMRV groups.

End point values	10Pn-MMRV Group	DTPa-HBV-IPV/Hib-MMRV Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	102	89		
Units: Subjects				
SCR Rubella, Day 42 (N=102;88)	102	86		
SCR Rubella, Day 84 (N=102;89)	101	89		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seroconverted as regards antibodies against varicella antigens

End point title	Number of subjects seroconverted as regards antibodies against varicella antigens ^[16]
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End point description:

Seroconversion for varicella (SCR Varicella) was defined as a) appearance of antibody levels \geq the seropositivity assay cut-off of 4 (in titers) in seronegative subjects prior to dose 1 of MMRV vaccine or b) appearance of antibody levels \geq the seropositivity assay cut-off of 4 (in titers) in seronegative subjects prior to Dose 1 and 42-56 days after the first dose of MMRV vaccine (prior to Dose 2 of MMRV vaccine). Only the appearance of antibody levels \geq the seropositivity assay cut-off of 4 (in titers) as assessed at 42-56 days after the second dose of MMRV vaccine, and in seronegative subjects prior to Dose 1 was analysed and tabulated. A subject with seronegative levels of antibodies against varicella antigens was defined as a subject with anti-varicella antibody titer < 4 .

End point type	Secondary
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End point timeframe:

At Day 42 (42-56 days post 1st dose of MMRV vaccine) at Day 84 (42-56 days post 2nd dose of MMRV vaccine)

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: This endpoint was only analysed in the 10Pn-MMRV and DTPa-HBV-IPV/Hib-MMRV groups.

End point values	10Pn-MMRV Group	DTPa-HBV-IPV/Hib-MMRV Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	99	87		
Units: Subjects				
SCR Varicella, Day 42 (N=98;85)	98	83		
SCR Varicella, Day 84 (N=99;87)	99	87		

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of antibodies against measles antigens

End point title	Concentrations of antibodies against measles antigens ^[17]
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End point description:

The seropositivity cut-off for the assay was an anti-measles antibody (Anti-Measles Ab) concentration \geq 150 milli-international units per millilitre (mIU/mL).

End point type	Secondary
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End point timeframe:

At Day 42 (42-56 days post 1st dose of MMRV vaccine) at Day 84 (42-56 days post 2nd dose of MMRV vaccine).

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: This endpoint was only analysed in the 10Pn-MMRV and DTPa-HBV-IPV/Hib-MMRV groups.

End point values	10Pn-MMRV Group	DTPa-HBV-IPV/Hib-MMRV Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	102	89		
Units: mIU/mL				
geometric mean (confidence interval 95%)				
Anti-Measles Ab, Day 42 (N=102;88)	3740.2 (3181.7 to 4396.8)	2836.9 (2374 to 3390.1)		
Anti-Measles Ab, Day 84 (N=102;89)	4792.3 (4071.7 to 5640.5)	4331.6 (3716.8 to 5048.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of antibodies against mumps antigens

End point title	Concentrations of antibodies against mumps antigens ^[18]
End point description: The seropositivity cut-off for the assay was an anti-mumps antibody (Anti-Mumps Ab) concentration \geq 231 units per millilitre (U/mL).	
End point type	Secondary
End point timeframe: At Day 42 (42-56 days post 1st dose of MMRV vaccine) at Day 84 (42-56 days post 2nd dose of MMRV vaccine).	
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: This endpoint was only analysed in the 10Pn-MMRV and DTPa-HBV-IPV/Hib-MMRV groups.	

End point values	10Pn-MMRV Group	DTPa-HBV-IPV/Hib-MMRV Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	102	89		
Units: U/mL				
geometric mean (confidence interval 95%)				
Anti-Mumps Ab, Day 42 (N=102;88)	810.8 (667.3 to 985.1)	801 (648.5 to 989.4)		
Anti-Mumps Ab, Day 84 (N=102;89)	1132.7 (968.2 to 1325.2)	1411.2 (1210.1 to 1645.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of antibodies against rubella antigens

End point title	Concentrations of antibodies against rubella antigens ^[19]
End point description: The seropositivity cut-off for the assay was an anti-rubella antibody (Anti-Rubella Ab) concentration \geq 4 international units per millilitre (IU/mL).	
End point type	Secondary
End point timeframe: At Day 42 (42-56 days post 1st dose of MMRV vaccine) at Day 84 (42-56 days post 2nd dose of MMRV vaccine).	
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: This endpoint was only analysed in the 10Pn-MMRV and DTPa-HBV-IPV/Hib-MMRV groups.	

End point values	10Pn-MMRV Group	DTPa-HBV-IPV/Hib-MMRV Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	102	89		
Units: IU/mL				
geometric mean (confidence interval 95%)				
Anti-Rubella Ab, Day 42 (N=102;88)	39.5 (33.8 to 46.2)	33 (27 to 40.2)		
Anti-Rubella Ab, Day 84 (N=102;89)	78.4 (68.3 to 90)	85.9 (73.8 to 99.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of antibodies against varicella antigens

End point title	Concentrations of antibodies against varicella antigens ^[20]
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End point description:

The seropositivity cut-off for the assay was an anti-varicella antibody (Anti-Varicella Ab) titer ≥ 4

End point type	Secondary
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End point timeframe:

At Day 42 (42-56 days post 1st dose of MMRV vaccine) at Day 84 (42-56 days post 2nd dose of MMRV vaccine)

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: This endpoint was only analysed in the 10Pn-MMRV and DTPa-HBV-IPV/Hib-MMRV groups.

End point values	10Pn-MMRV Group	DTPa-HBV-IPV/Hib-MMRV Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	100	89		
Units: Titer				
geometric mean (confidence interval 95%)				
Anti-Varicella Ab, Day 42 (N=99;87)	124.5 (102.8 to 150.7)	115.4 (89.2 to 149.3)		
Anti-Varicella Ab, Day 84 (N=100;89)	1629.3 (1361.9 to 1949.1)	1583.8 (1290.8 to 1943.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with seropositive levels of antibodies against measles antigens

End point title	Number of subjects with seropositive levels of antibodies against measles antigens ^[21]
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End point description:

End point type	Secondary
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End point timeframe:

At Day 42 (42-56 days post 1st dose of MMRV vaccine) at Day 84 (42-56 days post 2nd dose of MMRV vaccine)

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: This endpoint was only analysed in the 10Pn-MMRV and DTPa-HBV-IPV/Hib-MMRV groups.

End point values	10Pn-MMRV Group	DTPa-HBV-IPV/Hib-MMRV Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	102	89		
Units: Subjects				
S+ Measles, Day 42 (N=102;88)	100	86		
S+ Measles, Day 84 (N=102;89)	101	89		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Fever as solicited general symptom (SGS): 15 days post vaccination. Solicited symptoms: 4 days post vaccination. SGSs specific to MMRV & unsolicited AEs: 43 days post vaccination. See below for SAEs timeframes.

Adverse event reporting additional description:

SAEs: 1) Active Phase: Day 0 to Day 86-112 (2 groups receiving MMRV)/ Day 42-56 (other group); 2) Entire study: Day 0 to Day 222-266 (2 groups receiving MMRV)/Day 180-210 (other group). The occurrence of reported AEs (all/related) was not available and is encoded as equal to the number of subjects affected.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	10.1

Reporting groups

Reporting group title	10Pn-MMRV Group
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Reporting group description:

This group consisted of subjects previously vaccinated with the 10Pn-PD-DiT (or 10Pn) vaccine during the 10PN-PD-DIT-001 (105553) study (EudraCT number: 2005-003300-11). In 105553 study, subjects had been primed with 3 doses of 10Pn vaccine at 2, 3 and 4 months of age (injected intramuscularly [IM] in the right thigh) co-administered with DTPa-HBV-IPV/Hib vaccine (or Infanrix hexa™), except for the 2nd dose in France, which was co-administered with DTPa-IPV/Hib (or Infanrix™ IPV Hib), injected IM in the left thigh. In this 107706 study, subjects received at 12 to 14 months of age a booster dose of 10Pn vaccine co-administered with the 1st dose of Priorix-Tetra™ (or MMRV vaccine), and, at 14 to 16 months of age, the 2nd dose of MMRV vaccine co-administered with a booster dose of DTPa-HBV-IPV/Hib vaccine. The 10Pn and DTPa-HBV-IPV/Hib vaccines were administered IM in the left thigh or deltoid and the MMRV vaccine subcutaneously in the right deltoid.

Reporting group title	DTPa-HBV-IPV/Hib-MMRV Group
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Reporting group description:

This group consisted of subjects previously vaccinated with the 10Pn-PD-DiT (or 10Pn) vaccine during the 10PN-PD-DIT-001 (105553) study (EudraCT number: 2005-003300-11). In the 105553 study, subjects had been primed with 3 doses of 10Pn vaccine at 2, 3 and 4 months of age (injected intramuscularly [IM] in the right thigh) co-administered with DTPa-HBV-IPV/Hib vaccine (or Infanrix hexa™), except for the 2nd dose in France, which was co-administered with DTPa-IPV/Hib (or Infanrix™ IPV Hib), injected IM in the left thigh. In this 107706 study, subjects received at 12 to 14 months of age a booster dose of DTPa-HBV-IPV/Hib vaccine co-administered with the 1st dose of Priorix-Tetra™ (or MMRV vaccine), and, at 14 to 16 months of age, the 2nd dose of MMRV vaccine co-administered with a booster dose of 10Pn vaccine. The 10Pn and DTPa-HBV-IPV/Hib vaccines were administered IM in the left thigh or deltoid and the MMRV vaccine subcutaneously in the right deltoid.

Reporting group title	10Pn-DTPa-HBV-IPV/Hib Group
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Reporting group description:

This group consisted of subjects previously vaccinated with the 10Pn-PD-DiT (or 10Pn) vaccine during the 10PN-PD-DIT-001 (105553) study (EudraCT number: 2005-003300-11). In the 105553 study, subjects had been primed with 3 doses of 10Pn vaccine at 2, 3 and 4 months of age (injected intramuscularly [IM] in the right thigh) co-administered with DTPa-HBV-IPV/Hib vaccine (or Infanrix hexa™), except for the second dose in France, which was co-administered with DTPa-IPV/Hib (or Infanrix™ IPV Hib), injected IM in the left thigh. In this 107706 study, subjects received at 12 to 14 months of age a booster dose of 10Pn vaccine co-administered with a booster dose of DTPa-HBV-IPV/Hib vaccine. The 10Pn and DTPa-HBV-IPV/Hib vaccines were administered IM in the thigh or deltoid, respectively in the left and right side.

Serious adverse events	10Pn-MMRV Group	DTPa-HBV-IPV/Hib-MMRV Group	10Pn-DTPa-HBV-IPV/Hib Group
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 110 (4.55%)	3 / 101 (2.97%)	4 / 114 (3.51%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Nervous system disorders			
Febrile convulsion (Entire Study)			
subjects affected / exposed ^[1]	0 / 108 (0.00%)	1 / 100 (1.00%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Bronchitis chronic (Active Phase)			
subjects affected / exposed	0 / 110 (0.00%)	0 / 101 (0.00%)	1 / 114 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis chronic (Entire Study)			
subjects affected / exposed ^[2]	1 / 108 (0.93%)	1 / 100 (1.00%)	1 / 111 (0.90%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Adenovirus infection (Active Phase)			
subjects affected / exposed	1 / 110 (0.91%)	0 / 101 (0.00%)	0 / 114 (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
Skin infection (Active Phase)			
subjects affected / exposed	1 / 110 (0.91%)	0 / 101 (0.00%)	0 / 114 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adenovirus infection (Entire Study)			
subjects affected / exposed ^[3]	1 / 108 (0.93%)	0 / 100 (0.00%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis (Entire Study)			

subjects affected / exposed ^[4]	1 / 108 (0.93%)	0 / 100 (0.00%)	0 / 111 (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
Exanthema subitum (Entire Study)			
subjects affected / exposed ^[5]	0 / 108 (0.00%)	0 / 100 (0.00%)	1 / 111 (0.90%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis (Entire Study)			
subjects affected / exposed ^[6]	0 / 108 (0.00%)	1 / 100 (1.00%)	1 / 111 (0.90%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis rotavirus (Entire Study)			
subjects affected / exposed ^[7]	1 / 108 (0.93%)	0 / 100 (0.00%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngitis (Entire Study)			
subjects affected / exposed ^[8]	0 / 108 (0.00%)	0 / 100 (0.00%)	1 / 111 (0.90%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin infection (Entire Study)			
subjects affected / exposed ^[9]	1 / 108 (0.93%)	0 / 100 (0.00%)	0 / 111 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Notes:

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

Justification: SAEs for the Entire Study period were only assessed in subjects participating to the ESFU Phase (that is, 108, 100 and 111 subjects in the 10Pn-MMRV, DTPa-HBV-IPV/Hib-MMRV and 10Pn-DTPa-HBV-IPV/Hib Groups, respectively).

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

Justification: SAEs for the Entire Study period were only assessed in subjects participating to the ESFU Phase (that is, 108, 100 and 111 subjects in the 10Pn-MMRV, DTPa-HBV-IPV/Hib-MMRV and 10Pn-DTPa-HBV-IPV/Hib Groups, respectively).

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

Justification: SAEs for the Entire Study period were only assessed in subjects participating to the ESFU Phase (that is, 108, 100 and 111 subjects in the 10Pn-MMRV, DTPa-HBV-IPV/Hib-MMRV and 10Pn-DTPa-HBV-IPV/Hib Groups, respectively).

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

Justification: SAEs for the Entire Study period were only assessed in subjects participating to the ESFU Phase (that is, 108, 100 and 111 subjects in the 10Pn-MMRV, DTPa-HBV-IPV/Hib-MMRV and 10Pn-DTPa-HBV-IPV/Hib Groups, respectively).

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

Justification: SAEs for the Entire Study period were only assessed in subjects participating to the ESFU Phase (that is, 108, 100 and 111 subjects in the 10Pn-MMRV, DTPa-HBV-IPV/Hib-MMRV and 10Pn-DTPa-HBV-IPV/Hib Groups, respectively).

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

Justification: SAEs for the Entire Study period were only assessed in subjects participating to the ESFU Phase (that is, 108, 100 and 111 subjects in the 10Pn-MMRV, DTPa-HBV-IPV/Hib-MMRV and 10Pn-DTPa-HBV-IPV/Hib Groups, respectively).

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

Justification: SAEs for the Entire Study period were only assessed in subjects participating to the ESFU Phase (that is, 108, 100 and 111 subjects in the 10Pn-MMRV, DTPa-HBV-IPV/Hib-MMRV and 10Pn-DTPa-HBV-IPV/Hib Groups, respectively).

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

Justification: SAEs for the Entire Study period were only assessed in subjects participating to the ESFU Phase (that is, 108, 100 and 111 subjects in the 10Pn-MMRV, DTPa-HBV-IPV/Hib-MMRV and 10Pn-DTPa-HBV-IPV/Hib Groups, respectively).

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

Justification: SAEs for the Entire Study period were only assessed in subjects participating to the ESFU Phase (that is, 108, 100 and 111 subjects in the 10Pn-MMRV, DTPa-HBV-IPV/Hib-MMRV and 10Pn-DTPa-HBV-IPV/Hib Groups, respectively).

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

Non-serious adverse events	10Pn-MMRV Group	DTPa-HBV-IPV/Hib-MMRV Group	10Pn-DTPa-HBV-IPV/Hib Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	101 / 110 (91.82%)	88 / 101 (87.13%)	84 / 114 (73.68%)
General disorders and administration site conditions			
Pain			
alternative assessment type: Systematic			
subjects affected / exposed ^[10]	69 / 109 (63.30%)	50 / 101 (49.50%)	73 / 112 (65.18%)
occurrences (all)	69	50	73
Redness			
alternative assessment type: Systematic			
subjects affected / exposed ^[11]	79 / 109 (72.48%)	75 / 101 (74.26%)	70 / 112 (62.50%)
occurrences (all)	79	75	70
Swelling			
alternative assessment type: Systematic			
subjects affected / exposed ^[12]	58 / 109 (53.21%)	57 / 101 (56.44%)	52 / 112 (46.43%)
occurrences (all)	58	57	52
Drowsiness			
alternative assessment type: Systematic			

subjects affected / exposed ^[13]	55 / 109 (50.46%)	54 / 101 (53.47%)	57 / 112 (50.89%)
occurrences (all)	55	54	57
Irritability			
alternative assessment type: Systematic			
subjects affected / exposed ^[14]	80 / 109 (73.39%)	73 / 101 (72.28%)	84 / 112 (75.00%)
occurrences (all)	80	73	84
Loss of appetite			
alternative assessment type: Systematic			
subjects affected / exposed ^[15]	47 / 109 (43.12%)	33 / 101 (32.67%)	37 / 112 (33.04%)
occurrences (all)	47	33	37
Temperature (rectally) > 39.0 °C			
alternative assessment type: Systematic			
subjects affected / exposed ^[16]	38 / 109 (34.86%)	34 / 101 (33.66%)	9 / 112 (8.04%)
occurrences (all)	38	34	9
Temperature (rectally) ≥ 38.0°C			
alternative assessment type: Systematic			
subjects affected / exposed ^[17]	101 / 109 (92.66%)	88 / 101 (87.13%)	69 / 112 (61.61%)
occurrences (all)	101	88	69
Rash			
subjects affected / exposed ^[18]	38 / 109 (34.86%)	48 / 101 (47.52%)	18 / 112 (16.07%)
occurrences (all)	38	48	18
Injection site induration (Unsolicited AE)			
subjects affected / exposed	5 / 110 (4.55%)	8 / 101 (7.92%)	10 / 114 (8.77%)
occurrences (all)	5	8	10
Irritability (Unsolicited AE)			
alternative assessment type: Systematic			
subjects affected / exposed	19 / 110 (17.27%)	14 / 101 (13.86%)	6 / 114 (5.26%)
occurrences (all)	19	14	6
Eye disorders			
Conjunctivitis (Unsolicited AE)			
subjects affected / exposed	10 / 110 (9.09%)	6 / 101 (5.94%)	6 / 114 (5.26%)
occurrences (all)	10	6	6
Gastrointestinal disorders			

Diarrhoea (Unsolicited AE) subjects affected / exposed occurrences (all)	17 / 110 (15.45%) 17	15 / 101 (14.85%) 15	9 / 114 (7.89%) 9
Teething (Unsolicited AE) subjects affected / exposed occurrences (all)	14 / 110 (12.73%) 14	14 / 101 (13.86%) 14	5 / 114 (4.39%) 5
Vomiting (Unsolicited AE) subjects affected / exposed occurrences (all)	7 / 110 (6.36%) 7	8 / 101 (7.92%) 8	3 / 114 (2.63%) 3
Respiratory, thoracic and mediastinal disorders Cough (Unsolicited AE) subjects affected / exposed occurrences (all)	15 / 110 (13.64%) 15	27 / 101 (26.73%) 27	7 / 114 (6.14%) 7
Infections and infestations Bronchitis (Unsolicited AE) subjects affected / exposed occurrences (all)	4 / 110 (3.64%) 4	5 / 101 (4.95%) 5	5 / 114 (4.39%) 5
Gastroenteritis (Unsolicited AE) subjects affected / exposed occurrences (all)	6 / 110 (5.45%) 6	5 / 101 (4.95%) 5	8 / 114 (7.02%) 8
Otitis media (Unsolicited AE) subjects affected / exposed occurrences (all)	26 / 110 (23.64%) 26	28 / 101 (27.72%) 28	18 / 114 (15.79%) 18
Respiratory tract infection (Unsolicited AE) subjects affected / exposed occurrences (all)	5 / 110 (4.55%) 5	5 / 101 (4.95%) 5	3 / 114 (2.63%) 3
Rhinitis (Unsolicited AE) subjects affected / exposed occurrences (all)	19 / 110 (17.27%) 19	30 / 101 (29.70%) 30	13 / 114 (11.40%) 13
Upper respiratory tract infection (Unsolicited AE) subjects affected / exposed occurrences (all)	27 / 110 (24.55%) 27	21 / 101 (20.79%) 21	18 / 114 (15.79%) 18
Metabolism and nutrition disorders Anorexia (Unsolicited AE)			

subjects affected / exposed	8 / 110 (7.27%)	2 / 101 (1.98%)	1 / 114 (0.88%)
occurrences (all)	8	2	1

Notes:

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

Justification: Assessment of solicited local and general symptoms was done in subjects with available results for the symptom specified.

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

Justification: Assessment of solicited local and general symptoms was done in subjects with available results for the symptom specified.

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

Justification: Assessment of solicited local and general symptoms was done in subjects with available results for the symptom specified.

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

Justification: Assessment of solicited local and general symptoms was done in subjects with available results for the symptom specified.

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

Justification: Assessment of solicited local and general symptoms was done in subjects with available results for the symptom specified.

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

Justification: Assessment of solicited local and general symptoms was done in subjects with available results for the symptom specified.

[16] - 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: Assessment of solicited local and general symptoms was done in subjects with available results for the symptom specified.

[17] - 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: Assessment of solicited local and general symptoms was done in subjects with available results for the symptom specified.

[18] - 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: Assessment of solicited local and general symptoms was done in subjects with available results for the symptom specified.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported