Clinical trial results:
A Phase 3, Open label, Multi-Center, Extension Study to Evaluate the Safety, Tolerability and Immunogenicity of Novartis Meningococcal B Recombinant Vaccine When Administered as a Booster at 12 Months of Age or as a Two-dose Catch-up to Healthy Toddlers Who Participated in Study V72P13

Summary

EudraCT number	2008-006301-17
Trial protocol	IT CZ FI DE AT
Global end of trial date	19 August 2010

Results information

Result version number	v1 (current)
This version publication date	11 May 2016
First version publication date	03 January 2015

Trial information

Trial identification

Sponsor protocol code	V72P13E1

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00847145
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Vaccines and Diagnostics, S.r.l
Sponsor organisation address	Via Fiorentina, 1, Siena, Italy, 53100
Public contact	Posting Director, Novartis Vaccines , RegistryContactVaccinesUS@novartis.com
Scientific contact	Posting Director, Novartis Vaccines , RegistryContactVaccinesUS@novartis.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000139-PIP01-07
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	05 November 2010
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	19 August 2010
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Demonstration of a sufficient immune response following a fourth (booster) dose of rMenB+OMV NZ administered at 12 months of age, either with or without concomitant
MMRV vaccination, to toddlers previously primed with three doses of rMenB+OMV NZ as infants in Study V72P13.

Protection of trial subjects:

This trial was performed with the ethical principles that have their origin in the Declaration of Helsinki, that are consistent with Good Clinical Practice (GCP) according to International Conference on Harmonisation (ICH) guidelines, the applicable regulatory requirements (s) for the country in which the study was conducted, and applicable standard operating procedures (SOPs). Specifically, this trial was conducted under a protocol reviewed and approved by the EC and by scientifically and medically qualified persons; the benefits of the study were in proportion to the risks; the rights and welfare of the subjects were respected; the physicians conducting the trial did not find the hazards to outweigh the potential benefits.

Background therapy:

N/A

Evidence for comparator:

N/A

Actual start date of recruitment	11 February 2009
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	6 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Czech Republic: 882
Country: Number of subjects enrolled	Finland: 823
Country: Number of subjects enrolled	Germany: 38
Country: Number of subjects enrolled	Italy: 451
Country: Number of subjects enrolled	Austria: 55
Worldwide total number of subjects	2249
EEA total number of subjects	2249

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)	2249
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:

Subjects were enrolled at 15 sites in Finland, 12 sites in Germany, 5 sites in Austria, 27 sites in Czech Republic and 6 sites in Italy.

Pre-assignment

Screening details:

All enrolled subjects were included in the trial.

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, Data analyst

Blinding implementation details:

This study was partially open label (groups 1a, 1b, 2a, and 2b) and partially observer-blind (groups 3a, 3b, 4a, 4b).

Arms

Are arms mutually exclusive?	Yes
Arm title	12B12M (1a)

Arm description:

Previously in the parent study subjects had received three doses of rMenB+OMV NZ and routine vaccine at 2, 4 and 6 months of age, respectively. These subjects received a booster (fourth) dose at 12 months of age concomitantly with one dose of MMRV vaccine in the present study.

Arm type	Experimental
Investigational medicinal product name	rMenB+OMV NZ
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 dose of 0.5 mL

Investigational medicinal product name	MMRV
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

1 dose of 0.5 mL

Arm title	12B13M (1b)

Arm description:

Previously in the parent study subjects had received three doses of rMenB+OMV NZ and routine vaccine at 2, 4 and 6 months of age, respectively. These subjects received a booster (fourth) dose at 12 months and one dose of MMRV vaccine at 13 months of age in the present study.

Arm type	Experimental

Investigational medicinal product name	MMRV
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

1 dose of 0.5 mL

Investigational medicinal product name	rMenB+OMV NZ
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 dose of 0.5 mL

Arm title	12M13B15B (2a)

Arm description:

Previously in the present study subjects had received routine vaccine at 2, 4 and 6 months of age respectively. These subjects received MMRV vaccine at 12 months of age and two catch-up doses of rMenB+OMV NZ vaccine at 13 and 15 months of age in the present study.

Arm type	Experimental
Investigational medicinal product name	rMenB+OMV NZ
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

2 doses of 0.5 mL

Investigational medicinal product name	MMRV
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

1 dose of 0.5 mL

Arm title	12M12B14B (2b)

Arm description:

Previously in the parent study subjects had received three doses of routine vaccine at 2, 4 and 6 months of age, respectively. These subjects received two catch-up doses of rMenB+OMV NZ at 12 and 14 months of age and one dose of MMRV vaccine given concomitantly at 12 months of age in the present study.

Arm type	Experimental
Investigational medicinal product name	rMenB+OMV NZ
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

2 doses of 0.5 mL

Investigational medicinal product name	MMRV
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Powder and solvent for solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

1 dose of 0.5 mL

Arm title	12B12M (3a)

Arm description:

Previously in the parent study subjects had received three doses of rMenB+OMV NZ and routine vaccinations at 2, 4 and 6 months of age respectively. These subjects had received one booster (fourth) dose of rMenB+OMV NZ at 12 months of age concomitantly with one dose of MMRV vaccine in the present study.

Arm type	Experimental
Investigational medicinal product name	rMenB+OMV NZ
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 dose of 0.5 mL

Investigational medicinal product name	MMRV
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

1 dose of 0.5 mL

Arm title	12B13M (3b)

Arm description:

Previously in the present study subjects had received three doses of rMenB+OMV NZ and routine vaccinations at 12 months of age respectively. These subjects one booster (fourth) dose of rMenB+OMV NZ at 12 months of age and one dose of MMRV vaccine at 13 months of age in the present study.

Arm type	Experimental
Investigational medicinal product name	rMenB+OMV NZ
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 dose of 0.5 mL

Investigational medicinal product name	MMRV
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

1 dose of 0.5 mL

Arm title	12B12M_C (4a)

Arm description:

Previously in the parent study subjects had received three doses of Meningococcal C vaccine and routine vaccine at 2, 4 and 6 months of age respectively. These subjects had received one single dose of rMenB+OMV NZ at 12 months of age concomitantly with one dose of MMRV vaccine in the present

study.

Arm type	Experimental
Investigational medicinal product name	rMenB+OMV NZ
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 dose of 0.5 mL

Investigational medicinal product name	MMRV
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for suspension for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

1 dose of 0.5 mL

Arm title	12B13M_C (4b)

Arm description:

Previously in the parent study subjects had received three doses of Meningococcal C vaccine and routine vaccine at 2, 4 and 6 months of age. These subjects received one single dose of rMenB+OMV NZ at 12 months of age and one dose of MMRV vaccine at 13 months of age in the present study.

Arm type	Experimental
Investigational medicinal product name	rMenB+OMV NZ
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 dose of 0.5 mL

Investigational medicinal product name	MMRV
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

1 dose of 0.5 mL

Number of subjects in period 1	12B12M (1a)	12B13M (1b)	12M13B15B (2a)
Started	629	633	285
Completed	623	627	274
Not completed	6	6	11
Consent withdrawn by subject	3	4	6
Adverse Event	-	1	1
Inappropriate Enrolment	-	-	-
Lost to follow-up	3	1	1

Protocol deviation	-	-	3

Number of subjects in period 1	12M12B14B (2b)	12B12M (3a)	12B13M (3b)
Started	117	137	156
Completed	116	131	152
Not completed	1	6	4
Consent withdrawn by subject	1	-	-
Adverse Event	-	-	-
Inappropriate Enrolment	-	1	-
Lost to follow-up	-	4	4
Protocol deviation	-	1	-

Number of subjects in period 1	12B12M_C (4a)	12B13M_C (4b)
Started	152	140
Completed	143	136
Not completed	9	4
Consent withdrawn by subject	1	1
Adverse Event	-	-
Inappropriate Enrolment	-	-
Lost to follow-up	8	2
Protocol deviation	-	1

Baseline characteristics

Reporting groups	
Reporting group title	12B12M (1a)
Reporting group description:	
Previously in the parent study subjects had received three doses of rMenB+OMV NZ and routine vaccine at 2, 4 and 6 months of age, respectively. These subjects received a booster (fourth) dose at 12 months of age concomitantly with one dose of MMRV vaccine in the present study.	
Reporting group title	12B13M (1b)
Reporting group description:	
Previously in the parent study subjects had received three doses of rMenB+OMV NZ and routine vaccine at 2, 4 and 6 months of age, respectively. These subjects received a booster (fourth) dose at 12 months and one dose of MMRV vaccine at 13 months of age in the present study.	
Reporting group title	12M13B15B (2a)
Reporting group description:	
Previously in the present study subjects had received routine vaccine at 2, 4 and 6 months of age respectively. These subjects received MMRV vaccine at 12 months of age and two catch-up doses of rMenB+OMV NZ vaccine at 13 and 15 months of age in the present study.	
Reporting group title	12M12B14B (2b)
Reporting group description:	
Previously in the parent study subjects had received three doses of routine vaccine at 2, 4 and 6 months of age, respectively. These subjects received two catch-up doses of rMenB+OMV NZ at 12 and 14 months of age and one dose of MMRV vaccine given concomitantly at 12 months of age in the present study.	
Reporting group title	12B12M (3a)
Reporting group description:	
Previously in the parent study subjects had received three doses of rMenB+OMV NZ and routine vaccinations at 2, 4 and 6 months of age respectively. These subjects had received one booster (fourth) dose of rMenB+OMV NZ at 12 months of age concomitantly with one dose of MMRV vaccine in the present study.	
Reporting group title	12B13M (3b)
Reporting group description:	
Previously in the present study subjects had received three doses of rMenB+OMV NZ and routine vaccinations at 12 months of age respectively. These subjects one booster (fourth) dose of rMenB+OMV NZ at 12 months of age and one dose of MMRV vaccine at 13 months of age in the present study.	
Reporting group title	12B12M_C (4a)
Reporting group description:	
Previously in the parent study subjects had received three doses of Meningococcal C vaccine and routine vaccine at 2, 4 and 6 months of age respectively. These subjects had received one single dose of rMenB+OMV NZ at 12 months of age concomitantly with one dose of MMRV vaccine in the present study.	
Reporting group title	12B13M_C (4b)
Reporting group description:	
Previously in the parent study subjects had received three doses of Meningococcal C vaccine and routine vaccine at 2, 4 and 6 months of age. These subjects received one single dose of rMenB+OMV NZ at 12 months of age and one dose of MMRV vaccine at 13 months of age in the present study.	

Reporting group values	12B12M (1a)	12B13M (1b)	12M13B15B (2a)
Number of subjects	629	633	285
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	12.3	12.3	12.3
standard deviation	± 0.5	± 0.5	± 0.5
Gender categorical			
Units: Subjects			
Female	290	330	131
Male	339	303	154

Reporting group values	12M12B14B (2b)	12B12M (3a)	12B13M (3b)
Number of subjects	117	137	156
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	12.3	12.2	12.2
standard deviation	± 0.5	± 0.5	± 0.4
Gender categorical			
Units: Subjects			
Female	55	75	81
Male	62	62	75

Reporting group values	12B12M_C (4a)	12B13M_C (4b)	Total
Number of subjects	152	140	2249
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	12.2	12.2	
standard deviation	± 0.5	± 0.4	-
Gender categorical			
Units: Subjects			
Female	62	73	1097
Male	90	67	1152

End points

End points reporting groups

Reporting group title	12B12M (1a)

Reporting group description:

Previously in the parent study subjects had received three doses of rMenB+OMV NZ and routine vaccine at 2, 4 and 6 months of age, respectively. These subjects received a booster (fourth) dose at 12 months of age concomitantly with one dose of MMRV vaccine in the present study.

Reporting group title	12B13M (1b)

Reporting group description:

Previously in the parent study subjects had received three doses of rMenB+OMV NZ and routine vaccine at 2, 4 and 6 months of age, respectively. These subjects received a booster (fourth) dose at 12 months and one dose of MMRV vaccine at 13 months of age in the present study.

Reporting group title	12M13B15B (2a)

Reporting group description:

Previously in the present study subjects had received routine vaccine at 2, 4 and 6 months of age respectively. These subjects received MMRV vaccine at 12 months of age and two catch-up doses of rMenB+OMV NZ vaccine at 13 and 15 months of age in the present study.

Reporting group title	12M12B14B (2b)

Reporting group description:

Previously in the parent study subjects had received three doses of routine vaccine at 2, 4 and 6 months of age, respectively. These subjects received two catch-up doses of rMenB+OMV NZ at 12 and 14 months of age and one dose of MMRV vaccine given concomitantly at 12 months of age in the present study.

Reporting group title	12B12M (3a)

Reporting group description:

Previously in the parent study subjects had received three doses of rMenB+OMV NZ and routine vaccinations at 2, 4 and 6 months of age respectively. These subjects had received one booster (fourth) dose of rMenB+OMV NZ at 12 months of age concomitantly with one dose of MMRV vaccine in the present study.

Reporting group title	12B13M (3b)

Reporting group description:

Previously in the present study subjects had received three doses of rMenB+OMV NZ and routine vaccinations at 12 months of age respectively. These subjects one booster (fourth) dose of rMenB+OMV NZ at 12 months of age and one dose of MMRV vaccine at 13 months of age in the present study.

Reporting group title	12B12M_C (4a)

Reporting group description:

Previously in the parent study subjects had received three doses of Meningococcal C vaccine and routine vaccine at 2, 4 and 6 months of age respectively. These subjects had received one single dose of rMenB+OMV NZ at 12 months of age concomitantly with one dose of MMRV vaccine in the present study.

Reporting group title	12B13M_C (4b)

Reporting group description:

Previously in the parent study subjects had received three doses of Meningococcal C vaccine and routine vaccine at 2, 4 and 6 months of age. These subjects received one single dose of rMenB+OMV NZ at 12 months of age and one dose of MMRV vaccine at 13 months of age in the present study.

Subject analysis set title	Enrolled Population
Subject analysis set type	Intention-to-treat

Subject analysis set description:

all subjects who were enrolled in this study irrespective of whether they have been randomized or not

Subject analysis set title	SBA Persistence Per Protocol Population (SBA PP Persistence)
Subject analysis set type	Per protocol

Subject analysis set description:

All subjects who:
- received all the relevant doses of vaccine in study V72P13;
- blood draw at one month after the third injection at 6 month of age (in study V72P13) and visit 1 blood draw in this study;

- had no major protocol violation as defined prior to analysis.

Subject analysis set title	SBA Booster Per Protocol Population (SBA PP Booster)
Subject analysis set type	Per protocol

Subject analysis set description:

All subjects who:
- received all the relevant doses of vaccine in study V72P13;
- received rMenB+OMV NZ booster dose;
- provided evaluable serum samples at one month after the booster dose (Group 1a, 1b) and at one month after the second dose (group 2a, 2b);
- blood draw at one month after the third injection at 6 month of age (in study V72P13) and visit 1 blood draw in this study;
- had no major protocol violation as defined prior to analysis.

Subject analysis set title	SBA Catch-up Per Protocol Population (SBA PP Catch-up)
Subject analysis set type	Per protocol

Subject analysis set description:

All subjects who:
- received all the relevant doses of vaccine in study V72P13;
- received two catch-up doses of rMenB+OMV NZ;
- provided evaluable serum samples at one month after the second catch-up dose (group 2a, 2b);
- blood draw at one month after the third injection at 6 month of age (in study V72P13) and visit 1 blood draw in this study;
- had no major protocol violation as defined prior to analysis.

Subject analysis set title	Routine246
Subject analysis set type	Sub-group analysis

Subject analysis set description:

combined Groups 12M13B15B and 12M12B14B

Subject analysis set title	MMRV Per Protocol Population (MMRV PP)
Subject analysis set type	Per protocol

Subject analysis set description:

All subjects who:
- received all the relevant doses of vaccine correctly in studies V72P13 and in the current study;
- provided evaluable serum samples;
- blood draw at one month after the third injection at 6 month of age (in study V72P13) and visit 1 blood draw in this study;
- had no major protocol violation as defined prior to analysis.

Subject analysis set title	Men246
Subject analysis set type	Sub-group analysis

Subject analysis set description:

combined Groups 12B12M (1a) and 12B13M (1b)

Subject analysis set title	12B13M
Subject analysis set type	Safety analysis

Subject analysis set description:

Combination of Groups 12B13M (1b) and 12B13M (3b).

Subject analysis set title	12B12M
Subject analysis set type	Safety analysis

Subject analysis set description:

Combination of Groups 12B12M (1a) and 12B12M (3a).

Subject analysis set title	Safety Population
Subject analysis set type	Safety analysis

Subject analysis set description:

All subjects in the exposed population who provided post-baseline safety data.

Primary: Percentages of Subjects With Serum Bactericidal Antibody Titers ≥1:5 After Receiving a Fourth (Booster) Dose of rMenB+OMV NZ Vaccination

End point title	Percentages of Subjects With Serum Bactericidal Antibody Titers ≥1:5 After Receiving a Fourth (Booster) Dose of rMenB+OMV NZ Vaccination[1][2]

End point description:

Immunogenicity was assessed in terms of the percentages of subjects with serum bactericidal antibody (SBA) titers ≥1:5 for which the lower limit of the two-sided 95% confidence interval (CI) was ≥75%, directed against N. Meningitidis serogroup B reference strains H44/76-SL, NZ98/254 and 5/99, one month after the fourth (booster) dose of meningococcal B vaccine, rMenB+OMV NZ, with or without the concomitant Measles, Mumps, Rubella, Varicella (MMRV) vaccine in toddlers who were previously vaccinated with three doses of rMenB+OMV NZ. The analysis was done on SBA PP Booster population.

End point type	Primary

End point timeframe:

One month after the fourth (booster) dose.

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: There was no statistical null hypothesis associated with this immunogenicity objective.

[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: There was no statistical null hypothesis associated with this immunogenicity objective.

End point values	12B12M (1a)	12B13M (1b)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	211	215		
Units: Percentages of Subjects				
number (confidence interval 95%)				
Strain 44/76-SL (Baseline) (N=211, 215)	81 (75 to 86)	82 (77 to 87)		
One month after booster (N=210, 212)	100 (98 to 100)	100 (98 to 100)		
Strain 5/99 (Baseline) (N=210, 213)	98 (95 to 99)	100 (97 to 100)		
One month after booster (N=209, 212)	100 (98 to 100)	100 (98 to 100)		
Strain NZ98/254 (Baseline) (N=211, 215)	19 (14 to 25)	24 (19 to 30)		
One month after booster (N=211, 213)	97 (93 to 99)	94 (90 to 97)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentages of Subjects With Antibody Response After Receiving the MMRV Vaccination

End point title	Percentages of Subjects With Antibody Response After Receiving the MMRV Vaccination[3]

End point description:

Immunogenicity of MMRV, when given concomitantly with the fourth (booster) dose of rMenB+OMV NZ vaccine at 12 months of age, was assessed in terms of percentages of subjects with antibody responses against MMRV vaccine to demonstrate non-inferiority to that of MMRV given alone,.
The specified cut-off levels for Measles, Mumps and Rubella antigens is ≥255mIU/mL, ≥10 U/mL and ≥10 IU/mL Enzyme Linked Immunosorbent Assay(ELISA) Antibody(Ab) units, respectively. For Varicella is ≥1.25 glycoprotein (gp) ELISA units/ml (seroconversion) and ≥5 gp ELISA units/ml (seroprotection).
The analysis was done on MMRV PP population.

End point type	Secondary

End point timeframe:

One month after the fourth (booster) dose.

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: There was no statistical null hypothesis associated with this immunogenicity objective.

End point values	12B12M (1a)	12M13B15B (2a)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	163	156		
Units: Percentages of Subjects				
number (confidence interval 95%)				
Measles (Schwarz, ≥255), Bas (N=152,147)	0 (0 to 2)	0 (0 to 2)		
2 months after MMRV vaccine (N=151,146)	98 (94 to 100)	99 (96 to 100)		
Mumps (RIT4385, ≥10), Bas (N=157,152)	0 (0 to 2)	0 (0 to 2)		
2 months after MMRV vaccine (N=156, 151)	96 (92 to 99)	96 (92 to 99)		
Rubella (Wistar RA 27/3, ≥10), Bas (N=163,156)	0 (0 to 2)	0 (0 to 2)		
2 months after MMRV vaccine (N=162, 155)	99 (96 to 100)	100 (98 to 100)		
Varicella (Oka, ≥1.25), Bas (N=147,141)	0 (0 to 2)	0 (0 to 3)		
2 months after MMRV vaccine (N=146, 140)	97 (93 to 99)	99 (95 to 100)		
Varicella (Oka, ≥5), Bas (N=147,141)	0 (0 to 2)	0 (0 to 3)		
VarII 2 months after MMRV vaccine (N=146, 140)	79 (71 to 85)	81 (73 to 87)		

Statistical analyses

Statistical analysis title	non-inferiority of MMRV

Statistical analysis description:

The immunogenicity in 12B12M (1a) group was considered non-inferior to that in group 12M13B15B (2a), if, for measles antigen (2 months after MMRV vaccine), the lower limit of the two-sided 95% CI for the difference in the percentages of subjects with antibody response or equal to the specified cut-off level for that antigen was greater than -10%.

Comparison groups	12B12M (1a) v 12M13B15B (2a)
Number of subjects included in analysis	319
Analysis specification	Pre-specified
Analysis type	non-inferiority[4]
Method	95% Clopper-Pearson Confidence Intervals
Parameter estimate	Percentage group difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5
upper limit	2

Notes:

[4] - For the vaccine antigens Measles, the specified cut-off level was ≥255mIU/Ml to be greater than -10%.

Statistical analysis title	non-inferiority of MMRV 2

Statistical analysis description:

The immunogenicity in 12B12M (1a) group was considered non-inferior to that in group 12M13B15B (2a), if, for the mumps antigen (2 months after MMRV vaccine), the lower limit of the two-sided 95% CI for the difference in the percentages of subjects with antibody response or equal to the specified cut-off level for that antigen was greater than -10%.

Comparison groups	12B12M (1a) v 12M13B15B (2a)
Number of subjects included in analysis	319
Analysis specification	Pre-specified
Analysis type	non-inferiority[5]
Method	95% Clopper-Pearson Confidence Intervals
Parameter estimate	Percentage group difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5
upper limit	5

Notes:

[5] - For the vaccine antigen mumps, the specified cut-off level was ≥10 Enzyme Linked Immunosorbent Assay(ELISA) Antibody (Ab) units to be greater than -10%.

Statistical analysis title	non-inferiority of MMRV 3

Statistical analysis description:

The immunogenicity in 12B12M (1a) group was considered non-inferior to that in group 12M13B15B (2a), if, for the rubella antigen (2 months after MMRV vaccine), the lower limit of the two-sided 95% CI for the difference in the percentages of subjects with antibody response or equal to the specified cut-off level for that antigen was greater than -10%.

Comparison groups	12B12M (1a) v 12M13B15B (2a)
Number of subjects included in analysis	319
Analysis specification	Pre-specified
Analysis type	non-inferiority[6]
Method	95% Clopper-Pearson Confidence Intervals
Parameter estimate	Percentage group difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4
upper limit	1

Notes:

[6] - For the vaccine antigen rubella, the specified cut-off level was ≥10 IU/mL to be greater than -10%.

Statistical analysis title	non-inferiority of MMRV 4

Statistical analysis description:

The immunogenicity in 12B12M (1a) group was considered non-inferior to that in group 12M13B15B (2a), if, for the varicella antigen (2 months after MMRV vaccine), the lower limit of the two-sided 95% CI for the difference in the percentages of subjects with antibody response or equal to the specified cut-off level for that antigen was greater than -10%.

Comparison groups	12B12M (1a) v 12M13B15B (2a)

Number of subjects included in analysis	319
Analysis specification	Pre-specified
Analysis type	non-inferiority[7]
Method	95% Clopper-Pearson Confidence Intervals
Parameter estimate	Percentage group difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6
upper limit	3

Notes:

[7] - For the vaccine antigen varicella, the specified cut-off level was ≥1.25 gp ELISA units/mL to be greater than -10%.

Statistical analysis title	non-inferiority of MMRV 5

Statistical analysis description:

The immunogenicity in 12B12M (1a) group was considered non-inferior to that in group 12M13B15B (2a), if, for the varicella antigen (2 months after MMRV vaccine), the lower limit of the two-sided 95% CI for the difference in the percentages of subjects with antibody response or equal to the specified cut-off level for that antigen was greater than -10%.

Comparison groups	12M13B15B (2a) v 12B12M (1a)
Number of subjects included in analysis	319
Analysis specification	Pre-specified
Analysis type	non-inferiority[8]
Method	95% Clopper-Pearson Confidence Intervals
Parameter estimate	Percentage group difference
Point estimate	-2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11
upper limit	7

Notes:

[8] - For the vaccine antigen varicella, the specified cut-off level was ≥5 gp ELISA units/mL (seroprotection) to be greater than -10%.

Secondary: Geometric Mean Titers After Receiving the Booster Dose of rMenB+OMV NZ Vaccination

End point title	Geometric Mean Titers After Receiving the Booster Dose of rMenB+OMV NZ Vaccination[9]

End point description:

The immune response following a fourth (booster) dose of rMenB+OMV NZ administered at 12 months of age, either with (12B12M (1a)) or without (12B13M (1b)) concomitant MMRV vaccination was assessed as human serum bactericidal antibody (hSBA) titer (GMTs) one month after the fourth dose of rMenB+OMV NZ, directed against N. meningitidis serogroup B reference strains H44/76, NZ98/254 and 5/99.
The analysis was done on the SBA PP Booster population.

End point type	Secondary

End point timeframe:

One month after the booster (fourth) dose.

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: There was no statistical null hypothesis associated with this immunogenicity objective.

End point values	12B12M (1a)	12B13M (1b)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	211	215		
Units: Titers				
geometric mean (confidence interval 95%)				
Strain 44/76-SL, Baseline (N=211,215)	11 (9.27 to 12)	10 (9.11 to 12)		
1 Month after Booster (N=210, 212)	139 (123 to 156)	119 (105 to 133)		
Strain 5/99, Baseline (N=210, 213)	81 (71 to 93)	81 (71 to 92)		
1 Month after Booster (N=209, 212)	1503 (1339 to 1686)	1429 (1274 to 1603)		
Strain NZ98/254, Baseline (N=211, 215)	2.07 (1.8 to 2.38)	2.21 (1.92 to 2.55)		
1 Month after Booster (N=211,213)	39 (33 to 46)	32 (27 to 37)		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titers at 12 months of age (predose 4) After Previously Receiving the Three Doses of rMenB+OMV NZ (Persistence)

End point title	Geometric Mean Titers at 12 months of age (predose 4) After Previously Receiving the Three Doses of rMenB+OMV NZ (Persistence)[10]

End point description:

The persistence of bactericidal antibodies at 12 months of age (pre-dose 4) in infants who previously received three doses of rMenB+OMV NZ in the parent study was assessed as hSBA GMTs directed against N. meningitidis serogroup B reference strains H44/76, NZ98/254 and 5/99.
The analysis was done on the SBA PP Persistence population.

End point type	Secondary

End point timeframe:

One month after third vaccination and pre dose fourth (booster) vaccination.

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: There was no statistical null hypothesis associated with this immunogenicity objective.

End point values	12B12M (1a)	12B13M (1b)	Men246	Routine246
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	139	133	272	51
Units: Titers				
geometric mean (confidence interval 95%)				
H44/76, 1M after 3rd vac. in parent study	91 (81 to 104)	83 (73 to 94)	87 (79 to 95)	1.19 (1.07 to 1.33)
Pre-Booster vac.in present study	11 (9 to 12)	10 (8.7 to 12)	10 (9.28 to 12)	1.08 (0.99 to 1.17)
5/99, 1M after 3rd vac. in parent study	615 (538 to 704)	620 (540 to 712)	617 (560 to 680)	1 (1 to 1)
5/99 Pre-Booster vac.in present study	85 (72 to 100)	79 (67 to 94)	82 (73 to 92)	1.03 (0.97 to 1.09)

NZ98/254 >3rd in parent study (.N=139,132,271,52)	12 (10 to 15)	14 (12 to 17)	13 (11 to 15)	1.07 (0.94 to 1.21)
Pre-booster in present study (N=139,132,271,52)	2.04 (1.72 to 2.43)	2.02 (1.69 to 2.42)	2.03 (1.79 to 2.3)	1 (1 to 1)

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titers After Receiving the Booster Dose and Single Dose of rMen+OMV NZ Vaccination (Induction of Immunological Memory)

End point title	Geometric Mean Titers After Receiving the Booster Dose and Single Dose of rMen+OMV NZ Vaccination (Induction of Immunological Memory)[11]

End point description:

The induction of immunological memory was assessed in toddlers who previously received three doses of rMenB+OMV NZ in Study V72P13, by comparing the SBA GMT response when administered of the fourth dose of rMenB+OMV NZ at 12 months of age (12B12M (1a)) to the response in naïve toddlers receiving a single dose of rMenB+OMV NZ at 12 months of age (12M12B14B).
Immunological memory and booster response were demonstrated if the lower limit of the two-sided 95% CI for the ratio of the SBA GMTs following a fourth dose of rMenB+OMV NZ at 12 months of age compared to the SBA GMTs following a single dose of rMenB+OMV NZ at 12 months of age was ≥ 2.0.
The analysis was done on the SBA PP Booster population.

End point type	Secondary

End point timeframe:

One month post vaccination and pre-booster (fourth) dose vaccination.

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: There was no statistical null hypothesis associated with this immunogenicity objective.

End point values	12B12M (1a)	12M12B14B (2b)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	211	72		
Units: Titers				
geometric mean (confidence interval 95%)				
Strain H44/76, Baseline (N=211,71)	11 (9.32 to 12)	1.18 (0.96 to 1.46)		
1 M after Booster or 1st rMenB (N=210, 71)	140 (123 to 159)	15 (12 to 19)		
Strain 5/99, Baseline (N=210, 71)	83 (73 to 93)	1 (0.81 to 1.24)		
1 M after Booster or 1sr rMenB (N=209, 72)	1538 (1337 to 1769)	58 (46 to 74)		
Strain NZ98/254, Baseline (N=211, 71)	2.05 (1.83 to 2.31)	1.03 (0.84 to 1.26)		
1M after Booster or 1st rMenB (N=211, 72)	39 (34 to 46)	4.18 (3.18 to 5.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentages of subjects with SBA titers ≥1:5 at 12 months of age (predose 4) After Previously Receiving the Three Doses of rMenB+OMV NZ (Persistence)

End point title	Percentages of subjects with SBA titers ≥1:5 at 12 months of age (predose 4) After Previously Receiving the Three Doses of rMenB+OMV NZ (Persistence)[12]

End point description:

The persistence of bactericidal antibodies at 12 months of age (pre-dose 4) in infants who previously received three doses of rMenB+OMV NZ in the parent study was assessed as the percentages of subjects with SBA titers ≥1:5, directed against N. meningitidis serogroup B reference strains H44/76, NZ98/254 and 5/99.
The analysis was done on the SBA PP Persistence population.

End point type	Secondary

End point timeframe:

One month after third vaccination and pre dose fourth (booster) vaccination.

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: There was no statistical null hypothesis associated with this immunogenicity objective.

End point values	12B12M (1a)	12B13M (1b)	Men246	Routine246
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	139	133	272	51
Units: Percentages of Subjects				
number (confidence interval 95%)				
H44/76, 1M after 3rd vac. in P13	100 (97 to 100)	99 (96 to 100)	100 (98 to 100)	0 (0 to 7)
Pre-booster vac. in P13E1	81 (73 to 87)	82 (74 to 88)	81 (76 to 86)	2 (0.05 to 10)
5/99, 1M after 3rd vac. in P13	100 (97 to 100)	99 (96 to 100)	100 (98 to 100)	0 (0 to 7)
5/99 Pre-booster vac. in P13E1	98 (94 to 100)	100 (97 to 100)	99 (97 to 100)	0 (0 to 7)
NZ98/254, 1M after 3rd v.. P13 (.N=139,132,271,52)	81 (74 to 87)	85 (78 to 90)	83 (78 to 87)	2 (0.049 to 10)
Pre-booster vac. in P13E1 (N=139,132,271,52)	21 (14 to 29)	20 (13 to 28)	20 (16 to 26)	0 (0 to 7)

Statistical analyses

No statistical analyses for this end point

Secondary: SBA GMTs after a two-dose catch-up schedule or two-dose schedule

End point title	SBA GMTs after a two-dose catch-up schedule or two-dose schedule[13]

End point description:

The immunogenicity of a two-dose catch-up schedule of rMenB+OMV NZ given at 13 and 15 months (12M13B15B) or 12 and 14 months (12M12B14B) to naïve toddlers was assessed by SBA GMTs one month after the second dose.
The analysis was done on the SBA PP Catch-up population.

End point type	Secondary

End point timeframe:

One month after the second dose

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: There was no statistical null hypothesis associated with this immunogenicity objective.

End point values	12M13B15B (2a)	12M12B14B (2b)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	164	68		
Units: Titers				
geometric mean (confidence interval 95%)				
Strain H44/76, Baseline (N=161,67)	1.24 (1.15 to 1.35)	1.22 (1.07 to 1.38)		
1 M after 2nd Vac. (N=163, 67)	271 (237 to 310)	248 (201 to 306)		
Strain 5/99, Baseline (N=160, 67)	1.06 (1 to 1.13)	1.03 (0.94 to 1.13)		
1 M after 2nd Vac. (N=164, 67)	599 (520 to 690)	627 (502 to 783)		
Strain NZ98/254, Baseline (N=162, 67)	1.03 (0.98 to 1.07)	1.03 (0.97 to 1.1)		
1M after 2nd Vac. (N=164, 68)	43 (38 to 49)	32 (26 to 40)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentages of subjects with SBA titers ≥1:5 after a two-dose catch-up schedule or two-dose schedule

End point title	Percentages of subjects with SBA titers ≥1:5 after a two-dose catch-up schedule or two-dose schedule[14]

End point description:

The immunogenicity of a two-dose catch-up schedule of rMenB+OMV NZ given at 13 and 15 months (12M13B15B) or 12 and 14 months (12M12B14B) to naïve toddlers was assessed as percentages of subjects with SBA titers ≥1:5 one month after the second dose.
The analysis was done on the SBA PP Catch-up population.

End point type	Secondary

End point timeframe:

One month after the second dose.

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: There was no statistical null hypothesis associated with this immunogenicity objective.

End point values	12M13B15B (2a)	12M12B14B (2b)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	164	68		
Units: Percentages of Subjects				
number (confidence interval 95%)				
Strain H44/76, Baseline (N=161,67)	5 (2 to 10)	3 (0 to 10)		
1 M after 2nd Vac. (N=163, 67)	100 (98 to 100)	100 (95 to 100)		
Strain 5/99, Baseline (N=160, 67)	1 (0 to 4)	1 (0.038 to 8)		
1 M after 2nd Vac. (N=164, 67)	100 (98 to 100)	100 (95 to 100)		
Strain NZ98/254, Baseline (N=162, 67)	1 (0.016 to 3)	0 (0 to 5)		
1M after 2nd Vac. (N=164, 68)	100 (98 to 100)	96 (88 to 99)		

Statistical analyses

No statistical analyses for this end point

Secondary: ELISA Geometric Mean Concentration against vaccine antigen 287-953 one month after the fourth (booster) dose given at 12 months

End point title	ELISA Geometric Mean Concentration against vaccine antigen 287-953 one month after the fourth (booster) dose given at 12 months[15]

End point description:

The immune response against vaccine antigen 287-953 was measured by ELISA, one month after the fourth (booster) dose given at 12 months of age (groups 12B12M (1a), 12B13M (1b).
The analysis was done on the SBA PP Booster population.

End point type	Secondary

End point timeframe:

One month after the fourth (booster) dose.

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: There was no statistical null hypothesis associated with this immunogenicity objective.

End point values	12B12M (1a)	12B13M (1b)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	213	216		
Units: IU/mL				
geometric mean (confidence interval 95%)				
Baseline (N=212,216)	390 (351 to 433)	389 (349 to 434)		
1 M after Booster (N=213, 214)	6225 (5571 to 6956)	5608 (5111 to 6154)		

Statistical analyses

No statistical analyses for this end point

Secondary: ELISA Geometric Mean Concentration against vaccine antigen 287-953 after two-dose catch-up in toddlers

End point title	ELISA Geometric Mean Concentration against vaccine antigen 287-953 after two-dose catch-up in toddlers[16]

End point description:

The immune response against vaccine antigen 287-953was measured by ELISA one month after the first dose and one month after the second dose of a two-dose catch-up regimens (12M13B15B and 12M12B14B) in toddlers.
The analysis was done on the SBA PP Catch-up population.

End point type	Secondary

End point timeframe:

One month after the first dose and one month after the second dose

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: There was no statistical null hypothesis associated with this immunogenicity objective.

End point values	12M13B15B (2a)	12M12B14B (2b)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	165	68		
Units: IU/mL				
geometric mean (confidence interval 95%)				
Baseline (N=162,66)	20 (20 to 21)	22 (19 to 24)		
1 M after 1st Vac. (N=162,64)	113 (95 to 136)	120 (88 to 164)		
1 M after 2nd Vac.	5698 (5030 to 6454)	7154 (5880 to 8704)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentages of Subjects with Bactericidal Titers ≥ 1:5 (95% CI) Against Strain M10713 one month after the fourth (booster) dose given at 12 months

End point title	Percentages of Subjects with Bactericidal Titers ≥ 1:5 (95% CI) Against Strain M10713 one month after the fourth (booster) dose given at 12 months[17]

End point description:

The immune response was measured as percentages of subjects with SBA ≥ 1:5 (95% CI) against strain M10713, one month after the fourth (booster) dose given at 12 months of age (groups 12B12M (1a), 12B13M (1b).
The analysis was done on the SBA PP Booster population

End point type	Secondary

End point timeframe:

One month after the fourth (booster) dose.

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: There was no statistical null hypothesis associated with this immunogenicity objective.

End point values	12B12M (1a)	12B13M (1b)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	27		
Units: Percentages of Subjects				
number (confidence interval 95%)				
Pre-Booster Vac.	84 (60 to 97)	59 (39 to 78)		
1 Month After Booster	100 (82 to 100)	100 (87 to 100)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting solicited local and systemic reactions during the 7 days following rMenB+OMV NZ vaccination at 12 months of age

End point title	Number of subjects reporting solicited local and systemic reactions during the 7 days following rMenB+OMV NZ vaccination at 12 months of age[18]

End point description:

Safety was assessed as the number of subjects who reported solicited local and systemic reactions from day 1 through day 7 after rMenB+OMV NZ vaccination administered at 12 months. For the safety analysis purpose, Groups 12B12M (1a) and 12B12M (3a) are combined as Group 12B12M and Groups 12B13M (1b) and 12B13M (3b) are combined as Group 12B13M.
Analysis performed on the Safety population.

End point type	Secondary

End point timeframe:

From day 1 to day 7 after each rMenB+MV NZ vaccination.

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: All safety analyses were run in the safety population.

End point values	12B12M_C (4a)	12B13M_C (4b)	12B12M	12B13M
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	152	138	765	789
Units: Subjects				
Any local	113	104	639	673
MenB Tenderness	97	80	546	563
MenB Erythema	78	81	504	539
MenB Induration	61	61	388	424
MenB Swelling	44	39	284	287
Any systemic	133	117	695	671
Change Eat. Habits	61	44	312	318
Sleepiness	64	60	362	355

Vomiting	9	10	54	36
Diarrhea	29	23	188	160
Irritability	89	75	560	540
Unusual Crying	48	48	327	294
Rash	8	7	57	56
Rash Oth.to Fever	6	0	31	0
Rash Urt.to Fever	2	0	18	0
Rash Oth.to Doc.	6	0	35	0
Rash Urt.to Doc.	2	0	23	0
Gland Swelling	4	0	12	0
Gland Par.to Doc.	0	0	0	0
Gland Sal.to Doc.	0	0	0	0
Med. Att. Fever	3	4	8	13
Fever (≥ 38C)	87	74	356	325
Antipyr. Med. Used	79	69	436	406

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting solicited local and systemic reactions during the 7 days following two-dose catch-up schedules of rMenB+OMV NZ vaccination

End point title	Number of subjects reporting solicited local and systemic reactions during the 7 days following two-dose catch-up schedules of rMenB+OMV NZ vaccination[19]

End point description:

Safety was assessed as the number of subjects who reported solicited local and systemic reactions from day 1 through day 7 after rMenB+OMV NZ vaccination administered with a two-dose catch-up schedules (groups 12M13B15B and 12M12B14B).
Analysis performed on the Safety population.

End point type	Secondary

End point timeframe:

From day 1 to day 7 after each rMenB+MV NZ vaccination

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: All safety analyses were run in the safety population.

End point values	12M13B15B (2a)	12M12B14B (2b)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	284	117		
Units: Subjects				
Any local (1st vacc)	211	92		
Any local (2nd vacc)	212	90		
MenB Tenderness (1st vacc)	158	67		
MenB Tenderness (2nd vacc)	181	78		
MenB Erythema (1st vacc)	173	79		
MenB Erythema (2nd vacc)	159	70		

MenB Induration (1st vacc)	111	57		
MenB Induration (2nd vacc)	115	53		
MenB Swelling (1st vacc)	81	36		
MenB Swelling (2nd vacc)	83	33		
Any systemic (1st vacc)	216	104		
Any systemic (2nd vacc)	224	99		
Change Eat. Habits (1st vacc)	96	44		
Change Eat. Habits (2nd vacc)	83	43		
Sleepiness (1st vacc)	110	55		
Sleepiness (2nd vacc)	106	48		
Vomiting (1st vacc)	14	2		
Vomiting (2nd vacc)	8	3		
Diarrhea (1st vacc)	41	34		
Diarrhea (2nd vacc)	41	25		
Irritability (1st vacc)	168	82		
Irritability (2nd vacc)	153	73		
Unusual Crying (1st vacc)	80	41		
Unusual Crying (2nd vacc)	74	42		
Rash (1st vacc)	13	9		
Rash (2nd vacc)	10	4		
Rash Oth.to Fever (1st vacc)	0	0		
Rash Oth.to Fever (2nd vacc)	0	0		
Rash Urt.to Fever (1st vacc)	0	0		
Rash Urt.to Fever (2nd vacc)	0	0		
Rash Oth.to Doc. (1st vacc)	0	0		
Rash Oth.to Doc. (2nd vacc)	0	0		
Rash Urt.to Doc. (1st vacc)	0	0		
Rash Urt.to Doc. (2nd vacc)	0	0		
Gland Swelling (1st vacc)	0	1		
Gland Swelling (2nd vacc)	0	0		
Gland Par.to Doc. (1st vacc)	0	0		
Gland Par.to Doc. (2nd vacc)	0	0		
Gland Sal.to Doc. (1st vacc)	0	0		
Gland Sal.to Doc. (2nd vacc)	0	0		
Med. Att. Fever (1st vacc)	0	1		
Med. Att. Fever (2nd vacc)	2	2		
Fever (≥ 38C) (1st vacc)	103	54		
Fever (≥ 38C) (2nd vacc)	97	50		
Antipyr. Med. Used (1st vacc)	119	67		
Antipyr. Med. Used (2nd vacc)	107	58		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting solicited local reactions during the 7 days following MMRV vaccination at 12 months of age

End point title	Number of subjects reporting solicited local reactions during the 7 days following MMRV vaccination at 12 months of age[20]

End point description:

Safety was assessed as the number of subjects who reported solicited local reactions from day 1 through day 7 after the MMRV vaccination concomitantly with rMenB+OMV NZ at 12 months of age (groups 12B12M, 12M12B14B, 12B12M_C) or after MMRV vaccination alone without rMenB+OMV NZ at 12 months (Group 12M13B15B). For the safety analysis purpose, Groups 12B12M (1a) and 12B12M (3a) are combined as Group 12B12M.
Analysis performed on the Safety population.

End point type	Secondary

End point timeframe:

From day 1 to day 7 after MMRV vaccination

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: All safety analyses were run in the safety population.

End point values	12M13B15B (2a)	12M12B14B (2b)	12B12M_C (4a)	12B12M
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	284	117	152	760
Units: Subjects				
MMRV Tenderness	56	39	68	353
MMRV Erythema	120	52	60	345
MMRV Induration	53	18	30	161
MMRV Swelling	31	11	28	122

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting solicited systemic reactions during 8-28 days following MMRV vaccination at 12 months of age

End point title	Number of subjects reporting solicited systemic reactions during 8-28 days following MMRV vaccination at 12 months of age[21]

End point description:

Safety was assessed as the number of subjects who reported solicited systemic reactions from day 8 through day 28 after the MMRV vaccination concomitantly with rMenB+OMV NZ at 12 months of age (groups 12B12M, 12M12B14B, 12B12M_C) or after MMRV vaccination alone without rMenB+OMV NZ at 12 months (Group 12M13B15B). For the safety analysis purpose, Groups 12B12M (1a) and 12B12M (3a) are combined as Group 12B12M.
Analysis performed on the Safety population.

End point type	Secondary

End point timeframe:

From day 8 to day 28 after MMRV vaccination.

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: All safety analyses were run in the safety population.

End point values	12M13B15B (2a)	12M12B14B (2b)	12B12M_C (4a)	12B12M
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	284	117	152	760
Units: Subjects				
Rash	50	23	17	147
Rash Oth.to Fever	6	3	4	19
Rash Urt.to Fever	4	1	2	14
Rash Oth.to Doc.	3	1	3	10
Rash Urt.to Doc.	2	1	1	8
Gland Swelling	8	3	5	20
Gland Par.to Doc.	1	0	1	3
Gland Sal.to Doc.	1	0	1	5
Med. Att. Fever	19	6	15	54
Fever (≥ 38C)	131	46	62	338
Antipyr. Med. Used	119	55	48	324

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All solicited and unsolicited AEs were collected from Day 1 to 7; serious adverse events (SAEs), possibly or probably related, unrelated to vaccine, medically attended and leading to premature withdrawal AEs were collected during the overall study period.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	11.1

Reporting groups

Reporting group title	12B12M

Reporting group description:

Previously in the parent study subjects had received three doses of rMenB+OMV NZ and routine vaccine at 2, 4 and 6 months of age, respectively. These subjects received a booster (fourth) dose at 12 months of age concomitantly with one dose of MMRV vaccine in the present study. This group is a combination of Groups 12B12M (1a) and 12B12M (3a) for safety data analysis purposes.

Reporting group title	12B13M

Reporting group description:

Previously in the parent study subjects had received three doses of rMenB+OMV NZ and routine vaccine at 2, 4 and 6 months of age, respectively. These subjects received a booster (fourth) dose at 12 months and one dose of MMRV vaccine at 13 months of age in the present study. This group is a combination of Groups 12B13M (1b) and 12B13M (3b) for safety data analysis purposes.

Reporting group title	12M13B15B (2a)

Reporting group description:

Previously in the present study subjects had received routine vaccine at 2, 4 and 6 months of age respectively. These subjects received MMRV vaccine at 12 months of age and two catch-up doses of rMenB+OMV NZ vaccine at 13 and 15 months of age in the present study.

Reporting group title	12M12B14B (2b)

Reporting group description:

Previously in the parent study subjects had received three doses of routine vaccine at 2, 4 and 6 months of age, respectively. These subjects received two catch-up doses of rMenB+OMV NZ at 12 and 14 months of age and one dose of MMRV vaccine given concomitantly at 12 months of age in the present study.

Reporting group title	12B12M_C (4a)

Reporting group description:

Previously in the parent study subjects had received three doses of Meningococcal C vaccine and routine vaccine at 2, 4 and 6 months of age respectively. These subjects had received one single dose of rMenB+OMV NZ at 12 months of age concomitantly with one dose of MMRV vaccine in the present study.

Reporting group title	12B13M_C (4b)

Reporting group description:

Previously in the parent study subjects had received three doses of Meningococcal C vaccine and routine vaccine at 2, 4 and 6 months of age. These subjects received one single dose of rMenB+OMV NZ at 12 months of age and one dose of MMRV vaccine at 13 months of age in the present study.

Serious adverse events	12B12M	12B13M	12M13B15B (2a)
Total subjects affected by serious adverse events			
subjects affected / exposed	28 / 765 (3.66%)	40 / 789 (5.07%)	27 / 284 (9.51%)
number of deaths (all causes)	0	0	0
number of deaths resulting from	0	0	0

adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Haemangioma			
subjects affected / exposed	0 / 765 (0.00%)	0 / 789 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemangioma of skin			
subjects affected / exposed	0 / 765 (0.00%)	1 / 789 (0.13%)	0 / 284 (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
Vascular disorders			
Kawasaki's disease			
subjects affected / exposed	0 / 765 (0.00%)	0 / 789 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Strabismus correction			
subjects affected / exposed	0 / 765 (0.00%)	1 / 789 (0.13%)	0 / 284 (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
General disorders and administration site conditions			
Dysplasia			
subjects affected / exposed	0 / 765 (0.00%)	0 / 789 (0.00%)	0 / 284 (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
Hernia			
subjects affected / exposed	0 / 765 (0.00%)	0 / 789 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	1 / 765 (0.13%)	0 / 789 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			

Hypersensitivity			
subjects affected / exposed	0 / 765 (0.00%)	1 / 789 (0.13%)	0 / 284 (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			
Asthma			
subjects affected / exposed	1 / 765 (0.13%)	1 / 789 (0.13%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Accidental exposure to product			
subjects affected / exposed	0 / 765 (0.00%)	1 / 789 (0.13%)	0 / 284 (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
Burns second degree			
subjects affected / exposed	0 / 765 (0.00%)	1 / 789 (0.13%)	0 / 284 (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
Concussion			
subjects affected / exposed	1 / 765 (0.13%)	2 / 789 (0.25%)	0 / 284 (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
Contusion			
subjects affected / exposed	0 / 765 (0.00%)	1 / 789 (0.13%)	0 / 284 (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
Fall			
subjects affected / exposed	1 / 765 (0.13%)	1 / 789 (0.13%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			

subjects affected / exposed	0 / 765 (0.00%)	1 / 789 (0.13%)	0 / 284 (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
Foreign body aspiration			
subjects affected / exposed	0 / 765 (0.00%)	0 / 789 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Head injury			
subjects affected / exposed	0 / 765 (0.00%)	0 / 789 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mouth injury			
subjects affected / exposed	1 / 765 (0.13%)	0 / 789 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thermal burn			
subjects affected / exposed	0 / 765 (0.00%)	1 / 789 (0.13%)	0 / 284 (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
Congenital, familial and genetic disorders			
Cryptorchism			
subjects affected / exposed	0 / 765 (0.00%)	0 / 789 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydrocele			
subjects affected / exposed	0 / 765 (0.00%)	1 / 789 (0.13%)	0 / 284 (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
Phimosis			
subjects affected / exposed	0 / 765 (0.00%)	0 / 789 (0.00%)	0 / 284 (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
Nervous system disorders			

Ataxia			
subjects affected / exposed	0 / 765 (0.00%)	0 / 789 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Convulsion			
subjects affected / exposed	0 / 765 (0.00%)	1 / 789 (0.13%)	0 / 284 (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
Febrile convulsion			
subjects affected / exposed	4 / 765 (0.52%)	1 / 789 (0.13%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	1 / 4	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Loss of consciousness			
subjects affected / exposed	0 / 765 (0.00%)	0 / 789 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Partial seizures			
subjects affected / exposed	1 / 765 (0.13%)	0 / 789 (0.00%)	0 / 284 (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
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	1 / 765 (0.13%)	0 / 789 (0.00%)	0 / 284 (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
Abdominal pain			
subjects affected / exposed	1 / 765 (0.13%)	0 / 789 (0.00%)	0 / 284 (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
Colitis ulcerative			
subjects affected / exposed	0 / 765 (0.00%)	0 / 789 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspepsia			

subjects affected / exposed	0 / 765 (0.00%)	0 / 789 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enteritis			
subjects affected / exposed	0 / 765 (0.00%)	1 / 789 (0.13%)	0 / 284 (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
Enterocolitis			
subjects affected / exposed	2 / 765 (0.26%)	0 / 789 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	0 / 765 (0.00%)	1 / 789 (0.13%)	0 / 284 (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
Rash			
subjects affected / exposed	0 / 765 (0.00%)	0 / 789 (0.00%)	0 / 284 (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
Urticaria			
subjects affected / exposed	0 / 765 (0.00%)	1 / 789 (0.13%)	0 / 284 (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
Renal and urinary disorders			
Ureteric stenosis			
subjects affected / exposed	0 / 765 (0.00%)	0 / 789 (0.00%)	0 / 284 (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
Vesicoureteric reflux			
subjects affected / exposed	1 / 765 (0.13%)	0 / 789 (0.00%)	0 / 284 (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
Musculoskeletal and connective tissue			

disorders			
Growth retardation			
subjects affected / exposed	0 / 765 (0.00%)	0 / 789 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Juvenile idiopathic arthritis			
subjects affected / exposed	0 / 765 (0.00%)	1 / 789 (0.13%)	0 / 284 (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
Pain in extremity			
subjects affected / exposed	0 / 765 (0.00%)	0 / 789 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abscess			
subjects affected / exposed	1 / 765 (0.13%)	0 / 789 (0.00%)	0 / 284 (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
Acute tonsillitis			
subjects affected / exposed	0 / 765 (0.00%)	1 / 789 (0.13%)	0 / 284 (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
Bacterial infection			
subjects affected / exposed	0 / 765 (0.00%)	1 / 789 (0.13%)	0 / 284 (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
Bronchitis			
subjects affected / exposed	6 / 765 (0.78%)	3 / 789 (0.38%)	3 / 284 (1.06%)
occurrences causally related to treatment / all	0 / 8	0 / 3	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopneumonia			
subjects affected / exposed	0 / 765 (0.00%)	3 / 789 (0.38%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Campylobacter gastroenteritis			
subjects affected / exposed	0 / 765 (0.00%)	0 / 789 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 765 (0.00%)	1 / 789 (0.13%)	0 / 284 (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
Cellulitis orbital			
subjects affected / exposed	1 / 765 (0.13%)	0 / 789 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epstein-Barr virus infection			
subjects affected / exposed	0 / 765 (0.00%)	0 / 789 (0.00%)	0 / 284 (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
Exanthema subitum			
subjects affected / exposed	0 / 765 (0.00%)	2 / 789 (0.25%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 765 (0.00%)	1 / 789 (0.13%)	2 / 284 (0.70%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis rotavirus			
subjects affected / exposed	0 / 765 (0.00%)	0 / 789 (0.00%)	0 / 284 (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
Laryngitis			
subjects affected / exposed	4 / 765 (0.52%)	4 / 789 (0.51%)	2 / 284 (0.70%)
occurrences causally related to treatment / all	0 / 4	0 / 4	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nasopharyngitis			

subjects affected / exposed	0 / 765 (0.00%)	0 / 789 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oral herpes			
subjects affected / exposed	0 / 765 (0.00%)	1 / 789 (0.13%)	0 / 284 (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
Otitis media			
subjects affected / exposed	0 / 765 (0.00%)	2 / 789 (0.25%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media chronic			
subjects affected / exposed	0 / 765 (0.00%)	1 / 789 (0.13%)	0 / 284 (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
Pneumococcal sepsis			
subjects affected / exposed	1 / 765 (0.13%)	1 / 789 (0.13%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 765 (0.00%)	4 / 789 (0.51%)	4 / 284 (1.41%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	1 / 765 (0.13%)	2 / 789 (0.25%)	0 / 284 (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
Salmonellosis			
subjects affected / exposed	0 / 765 (0.00%)	0 / 789 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillitis			

subjects affected / exposed	0 / 765 (0.00%)	0 / 789 (0.00%)	2 / 284 (0.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tracheitis			
subjects affected / exposed	0 / 765 (0.00%)	0 / 789 (0.00%)	0 / 284 (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
Tracheobronchitis			
subjects affected / exposed	1 / 765 (0.13%)	0 / 789 (0.00%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	1 / 765 (0.13%)	0 / 789 (0.00%)	0 / 284 (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
Urinary tract infection			
subjects affected / exposed	1 / 765 (0.13%)	1 / 789 (0.13%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			
subjects affected / exposed	1 / 765 (0.13%)	1 / 789 (0.13%)	0 / 284 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Weight gain poor			
subjects affected / exposed	0 / 765 (0.00%)	0 / 789 (0.00%)	1 / 284 (0.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	12M12B14B (2b)	12B12M_C (4a)	12B13M_C (4b)
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 117 (7.69%)	7 / 152 (4.61%)	2 / 139 (1.44%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Haemangioma			
subjects affected / exposed	0 / 117 (0.00%)	0 / 152 (0.00%)	0 / 139 (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
Haemangioma of skin			
subjects affected / exposed	0 / 117 (0.00%)	0 / 152 (0.00%)	0 / 139 (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
Vascular disorders			
Kawasaki's disease			
subjects affected / exposed	0 / 117 (0.00%)	0 / 152 (0.00%)	0 / 139 (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
Surgical and medical procedures			
Strabismus correction			
subjects affected / exposed	0 / 117 (0.00%)	0 / 152 (0.00%)	0 / 139 (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			
Dysplasia			
subjects affected / exposed	0 / 117 (0.00%)	1 / 152 (0.66%)	0 / 139 (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
Hernia			
subjects affected / exposed	0 / 117 (0.00%)	0 / 152 (0.00%)	0 / 139 (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
Pyrexia			
subjects affected / exposed	0 / 117 (0.00%)	0 / 152 (0.00%)	0 / 139 (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
Immune system disorders			
Hypersensitivity			

subjects affected / exposed	0 / 117 (0.00%)	0 / 152 (0.00%)	0 / 139 (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			
Asthma			
subjects affected / exposed	0 / 117 (0.00%)	0 / 152 (0.00%)	0 / 139 (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
Injury, poisoning and procedural complications			
Accidental exposure to product			
subjects affected / exposed	0 / 117 (0.00%)	0 / 152 (0.00%)	0 / 139 (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
Burns second degree			
subjects affected / exposed	0 / 117 (0.00%)	0 / 152 (0.00%)	0 / 139 (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
Concussion			
subjects affected / exposed	0 / 117 (0.00%)	0 / 152 (0.00%)	0 / 139 (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
Contusion			
subjects affected / exposed	0 / 117 (0.00%)	0 / 152 (0.00%)	0 / 139 (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
Fall			
subjects affected / exposed	0 / 117 (0.00%)	0 / 152 (0.00%)	0 / 139 (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
Femur fracture			
subjects affected / exposed	0 / 117 (0.00%)	0 / 152 (0.00%)	0 / 139 (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

Foreign body aspiration			
subjects affected / exposed	0 / 117 (0.00%)	0 / 152 (0.00%)	0 / 139 (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
Head injury			
subjects affected / exposed	1 / 117 (0.85%)	0 / 152 (0.00%)	0 / 139 (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
Mouth injury			
subjects affected / exposed	0 / 117 (0.00%)	0 / 152 (0.00%)	0 / 139 (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
Thermal burn			
subjects affected / exposed	1 / 117 (0.85%)	0 / 152 (0.00%)	0 / 139 (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
Congenital, familial and genetic disorders			
Cryptorchism			
subjects affected / exposed	0 / 117 (0.00%)	0 / 152 (0.00%)	0 / 139 (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
Hydrocele			
subjects affected / exposed	0 / 117 (0.00%)	0 / 152 (0.00%)	0 / 139 (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
Phimosis			
subjects affected / exposed	1 / 117 (0.85%)	0 / 152 (0.00%)	0 / 139 (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
Nervous system disorders			
Ataxia			
subjects affected / exposed	0 / 117 (0.00%)	0 / 152 (0.00%)	0 / 139 (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

Convulsion			
subjects affected / exposed	0 / 117 (0.00%)	0 / 152 (0.00%)	0 / 139 (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
Febrile convulsion			
subjects affected / exposed	1 / 117 (0.85%)	1 / 152 (0.66%)	1 / 139 (0.72%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Loss of consciousness			
subjects affected / exposed	0 / 117 (0.00%)	0 / 152 (0.00%)	0 / 139 (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
Partial seizures			
subjects affected / exposed	0 / 117 (0.00%)	0 / 152 (0.00%)	0 / 139 (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
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 117 (0.00%)	0 / 152 (0.00%)	0 / 139 (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
Abdominal pain			
subjects affected / exposed	0 / 117 (0.00%)	0 / 152 (0.00%)	0 / 139 (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
Colitis ulcerative			
subjects affected / exposed	0 / 117 (0.00%)	0 / 152 (0.00%)	0 / 139 (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
Dyspepsia			
subjects affected / exposed	0 / 117 (0.00%)	0 / 152 (0.00%)	0 / 139 (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
Enteritis			

subjects affected / exposed	1 / 117 (0.85%)	0 / 152 (0.00%)	0 / 139 (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
Enterocolitis			
subjects affected / exposed	0 / 117 (0.00%)	0 / 152 (0.00%)	0 / 139 (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
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	0 / 117 (0.00%)	0 / 152 (0.00%)	0 / 139 (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
Rash			
subjects affected / exposed	1 / 117 (0.85%)	0 / 152 (0.00%)	0 / 139 (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
Urticaria			
subjects affected / exposed	0 / 117 (0.00%)	0 / 152 (0.00%)	0 / 139 (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
Renal and urinary disorders			
Ureteric stenosis			
subjects affected / exposed	0 / 117 (0.00%)	1 / 152 (0.66%)	0 / 139 (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
Vesicoureteric reflux			
subjects affected / exposed	0 / 117 (0.00%)	0 / 152 (0.00%)	0 / 139 (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
Musculoskeletal and connective tissue disorders			
Growth retardation			
subjects affected / exposed	0 / 117 (0.00%)	0 / 152 (0.00%)	0 / 139 (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

Juvenile idiopathic arthritis			
subjects affected / exposed	0 / 117 (0.00%)	0 / 152 (0.00%)	0 / 139 (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
Pain in extremity			
subjects affected / exposed	0 / 117 (0.00%)	0 / 152 (0.00%)	0 / 139 (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			
Abscess			
subjects affected / exposed	0 / 117 (0.00%)	0 / 152 (0.00%)	0 / 139 (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
Acute tonsillitis			
subjects affected / exposed	0 / 117 (0.00%)	0 / 152 (0.00%)	0 / 139 (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
Bacterial infection			
subjects affected / exposed	0 / 117 (0.00%)	0 / 152 (0.00%)	0 / 139 (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 / 117 (0.00%)	1 / 152 (0.66%)	0 / 139 (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
Bronchopneumonia			
subjects affected / exposed	0 / 117 (0.00%)	1 / 152 (0.66%)	0 / 139 (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
Campylobacter gastroenteritis			
subjects affected / exposed	0 / 117 (0.00%)	1 / 152 (0.66%)	0 / 139 (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
Cellulitis			

subjects affected / exposed	0 / 117 (0.00%)	0 / 152 (0.00%)	0 / 139 (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
Cellulitis orbital			
subjects affected / exposed	0 / 117 (0.00%)	0 / 152 (0.00%)	0 / 139 (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
Epstein-Barr virus infection			
subjects affected / exposed	0 / 117 (0.00%)	1 / 152 (0.66%)	0 / 139 (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
Exanthema subitum			
subjects affected / exposed	0 / 117 (0.00%)	0 / 152 (0.00%)	0 / 139 (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
Gastroenteritis			
subjects affected / exposed	1 / 117 (0.85%)	1 / 152 (0.66%)	0 / 139 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis rotavirus			
subjects affected / exposed	1 / 117 (0.85%)	0 / 152 (0.00%)	0 / 139 (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			
subjects affected / exposed	1 / 117 (0.85%)	0 / 152 (0.00%)	0 / 139 (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
Nasopharyngitis			
subjects affected / exposed	0 / 117 (0.00%)	0 / 152 (0.00%)	0 / 139 (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
Oral herpes			

subjects affected / exposed	0 / 117 (0.00%)	0 / 152 (0.00%)	0 / 139 (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
Otitis media			
subjects affected / exposed	0 / 117 (0.00%)	1 / 152 (0.66%)	0 / 139 (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
Otitis media chronic			
subjects affected / exposed	0 / 117 (0.00%)	0 / 152 (0.00%)	0 / 139 (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
Pneumococcal sepsis			
subjects affected / exposed	0 / 117 (0.00%)	0 / 152 (0.00%)	0 / 139 (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
Pneumonia			
subjects affected / exposed	0 / 117 (0.00%)	0 / 152 (0.00%)	0 / 139 (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
Pyelonephritis			
subjects affected / exposed	0 / 117 (0.00%)	0 / 152 (0.00%)	0 / 139 (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
Salmonellosis			
subjects affected / exposed	1 / 117 (0.85%)	0 / 152 (0.00%)	0 / 139 (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
Tonsillitis			
subjects affected / exposed	0 / 117 (0.00%)	0 / 152 (0.00%)	0 / 139 (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
Tracheitis			

subjects affected / exposed	0 / 117 (0.00%)	0 / 152 (0.00%)	1 / 139 (0.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tracheobronchitis			
subjects affected / exposed	0 / 117 (0.00%)	0 / 152 (0.00%)	0 / 139 (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
Upper respiratory tract infection			
subjects affected / exposed	0 / 117 (0.00%)	0 / 152 (0.00%)	0 / 139 (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
Urinary tract infection			
subjects affected / exposed	0 / 117 (0.00%)	0 / 152 (0.00%)	0 / 139 (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
Viral infection			
subjects affected / exposed	0 / 117 (0.00%)	0 / 152 (0.00%)	0 / 139 (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
Metabolism and nutrition disorders			
Weight gain poor			
subjects affected / exposed	0 / 117 (0.00%)	0 / 152 (0.00%)	0 / 139 (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

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

Non-serious adverse events	12B12M	12B13M	12M13B15B (2a)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	754 / 765 (98.56%)	760 / 789 (96.32%)	282 / 284 (99.30%)
Nervous system disorders			
Somnolence			
subjects affected / exposed	362 / 765 (47.32%)	355 / 789 (44.99%)	178 / 284 (62.68%)
occurrences (all)	599	569	430
Blood and lymphatic system disorders			

Lymphadenopathy			
subjects affected / exposed	29 / 765 (3.79%)	4 / 789 (0.51%)	13 / 284 (4.58%)
occurrences (all)	48	4	24
General disorders and administration site conditions			
Crying			
subjects affected / exposed	327 / 765 (42.75%)	294 / 789 (37.26%)	132 / 284 (46.48%)
occurrences (all)	558	467	302
Injection site erythema			
subjects affected / exposed	549 / 765 (71.76%)	539 / 789 (68.31%)	213 / 284 (75.00%)
occurrences (all)	1891	1326	1018
Injection site induration			
subjects affected / exposed	419 / 765 (54.77%)	424 / 789 (53.74%)	165 / 284 (58.10%)
occurrences (all)	1392	1188	717
Injection site pain			
subjects affected / exposed	561 / 765 (73.33%)	563 / 789 (71.36%)	224 / 284 (78.87%)
occurrences (all)	1648	1107	759
Injection site swelling			
subjects affected / exposed	320 / 765 (41.83%)	287 / 789 (36.38%)	127 / 284 (44.72%)
occurrences (all)	874	667	418
Pyrexia			
subjects affected / exposed	511 / 765 (66.80%)	356 / 789 (45.12%)	208 / 284 (73.24%)
occurrences (all)	1136	560	584
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	194 / 765 (25.36%)	171 / 789 (21.67%)	92 / 284 (32.39%)
occurrences (all)	342	268	215
Teething			
subjects affected / exposed	13 / 765 (1.70%)	12 / 789 (1.52%)	20 / 284 (7.04%)
occurrences (all)	13	13	22
Vomiting			
subjects affected / exposed	56 / 765 (7.32%)	39 / 789 (4.94%)	38 / 284 (13.38%)
occurrences (all)	78	53	52
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	33 / 765 (4.31%)	46 / 789 (5.83%)	11 / 284 (3.87%)
occurrences (all)	45	51	13

Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	178 / 765 (23.27%)	65 / 789 (8.24%)	78 / 284 (27.46%)
occurrences (all)	310	104	141
Psychiatric disorders			
Irritability			
subjects affected / exposed	562 / 765 (73.46%)	540 / 789 (68.44%)	226 / 284 (79.58%)
occurrences (all)	1121	996	742
Eating disorder			
subjects affected / exposed	313 / 765 (40.92%)	318 / 789 (40.30%)	156 / 284 (54.93%)
occurrences (all)	630	582	444
Infections and infestations			
Bronchitis			
subjects affected / exposed	60 / 765 (7.84%)	62 / 789 (7.86%)	38 / 284 (13.38%)
occurrences (all)	72	78	45
Conjunctivitis			
subjects affected / exposed	46 / 765 (6.01%)	38 / 789 (4.82%)	22 / 284 (7.75%)
occurrences (all)	57	42	24
Ear infection			
subjects affected / exposed	49 / 765 (6.41%)	59 / 789 (7.48%)	20 / 284 (7.04%)
occurrences (all)	60	100	37
Exanthema subitum			
subjects affected / exposed	20 / 765 (2.61%)	27 / 789 (3.42%)	15 / 284 (5.28%)
occurrences (all)	21	27	15
Gastroenteritis			
subjects affected / exposed	21 / 765 (2.75%)	25 / 789 (3.17%)	11 / 284 (3.87%)
occurrences (all)	22	25	11
Laryngitis			
subjects affected / exposed	26 / 765 (3.40%)	27 / 789 (3.42%)	14 / 284 (4.93%)
occurrences (all)	26	29	19
Nasopharyngitis			
subjects affected / exposed	49 / 765 (6.41%)	62 / 789 (7.86%)	37 / 284 (13.03%)
occurrences (all)	62	81	48
Otitis media			
subjects affected / exposed	80 / 765 (10.46%)	79 / 789 (10.01%)	42 / 284 (14.79%)
occurrences (all)	121	133	56
Pharyngitis			

subjects affected / exposed	38 / 765 (4.97%)	54 / 789 (6.84%)	19 / 284 (6.69%)
occurrences (all)	41	64	21
Rhinitis			
subjects affected / exposed	30 / 765 (3.92%)	38 / 789 (4.82%)	26 / 284 (9.15%)
occurrences (all)	35	43	35
Upper respiratory tract infection			
subjects affected / exposed	67 / 765 (8.76%)	59 / 789 (7.48%)	51 / 284 (17.96%)
occurrences (all)	83	71	66
Viral infection			
subjects affected / exposed	33 / 765 (4.31%)	36 / 789 (4.56%)	23 / 284 (8.10%)
occurrences (all)	35	38	28

Non-serious adverse events	12M12B14B (2b)	12B12M_C (4a)	12B13M_C (4b)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	116 / 117 (99.15%)	145 / 152 (95.39%)	132 / 139 (94.96%)
Nervous system disorders			
Somnolence			
subjects affected / exposed	70 / 117 (59.83%)	64 / 152 (42.11%)	61 / 139 (43.88%)
occurrences (all)	154	99	91
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	4 / 117 (3.42%)	8 / 152 (5.26%)	1 / 139 (0.72%)
occurrences (all)	6	14	1
General disorders and administration site conditions			
Crying			
subjects affected / exposed	59 / 117 (50.43%)	48 / 152 (31.58%)	50 / 139 (35.97%)
occurrences (all)	140	86	83
Injection site erythema			
subjects affected / exposed	94 / 117 (80.34%)	92 / 152 (60.53%)	82 / 139 (58.99%)
occurrences (all)	476	316	179
Injection site induration			
subjects affected / exposed	78 / 117 (66.67%)	67 / 152 (44.08%)	62 / 139 (44.60%)
occurrences (all)	325	223	159
Injection site pain			
subjects affected / exposed	89 / 117 (76.07%)	104 / 152 (68.42%)	81 / 139 (58.27%)
occurrences (all)	377	329	165
Injection site swelling			

subjects affected / exposed	53 / 117 (45.30%)	54 / 152 (35.53%)	40 / 139 (28.78%)
occurrences (all)	177	166	94
Pyrexia			
subjects affected / exposed	85 / 117 (72.65%)	110 / 152 (72.37%)	80 / 139 (57.55%)
occurrences (all)	211	256	125
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	48 / 117 (41.03%)	31 / 152 (20.39%)	25 / 139 (17.99%)
occurrences (all)	101	57	38
Teething			
subjects affected / exposed	3 / 117 (2.56%)	2 / 152 (1.32%)	2 / 139 (1.44%)
occurrences (all)	3	2	2
Vomiting			
subjects affected / exposed	5 / 117 (4.27%)	11 / 152 (7.24%)	11 / 139 (7.91%)
occurrences (all)	7	12	21
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	7 / 117 (5.98%)	9 / 152 (5.92%)	11 / 139 (7.91%)
occurrences (all)	8	15	14
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	30 / 117 (25.64%)	22 / 152 (14.47%)	9 / 139 (6.47%)
occurrences (all)	61	46	13
Psychiatric disorders			
Irritability			
subjects affected / exposed	95 / 117 (81.20%)	89 / 152 (58.55%)	76 / 139 (54.68%)
occurrences (all)	300	199	142
Eating disorder			
subjects affected / exposed	63 / 117 (53.85%)	61 / 152 (40.13%)	45 / 139 (32.37%)
occurrences (all)	152	117	84
Infections and infestations			
Bronchitis			
subjects affected / exposed	13 / 117 (11.11%)	12 / 152 (7.89%)	6 / 139 (4.32%)
occurrences (all)	16	20	9
Conjunctivitis			

subjects affected / exposed	5 / 117 (4.27%)	7 / 152 (4.61%)	1 / 139 (0.72%)
occurrences (all)	5	8	2
Ear infection			
subjects affected / exposed	14 / 117 (11.97%)	14 / 152 (9.21%)	6 / 139 (4.32%)
occurrences (all)	19	18	9
Exanthema subitum			
subjects affected / exposed	3 / 117 (2.56%)	4 / 152 (2.63%)	2 / 139 (1.44%)
occurrences (all)	3	4	2
Gastroenteritis			
subjects affected / exposed	2 / 117 (1.71%)	5 / 152 (3.29%)	7 / 139 (5.04%)
occurrences (all)	2	6	7
Laryngitis			
subjects affected / exposed	7 / 117 (5.98%)	2 / 152 (1.32%)	6 / 139 (4.32%)
occurrences (all)	7	2	6
Nasopharyngitis			
subjects affected / exposed	19 / 117 (16.24%)	3 / 152 (1.97%)	7 / 139 (5.04%)
occurrences (all)	28	3	7
Otitis media			
subjects affected / exposed	10 / 117 (8.55%)	9 / 152 (5.92%)	7 / 139 (5.04%)
occurrences (all)	13	10	7
Pharyngitis			
subjects affected / exposed	6 / 117 (5.13%)	7 / 152 (4.61%)	5 / 139 (3.60%)
occurrences (all)	6	9	6
Rhinitis			
subjects affected / exposed	7 / 117 (5.98%)	3 / 152 (1.97%)	4 / 139 (2.88%)
occurrences (all)	7	3	5
Upper respiratory tract infection			
subjects affected / exposed	11 / 117 (9.40%)	8 / 152 (5.26%)	9 / 139 (6.47%)
occurrences (all)	14	12	11
Viral infection			
subjects affected / exposed	10 / 117 (8.55%)	1 / 152 (0.66%)	0 / 139 (0.00%)
occurrences (all)	11	1	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 February 2009	Change of planned subjects. Change of Groups with respect to the parent study V72P13. Modification to serology and blood samples schedule.
28 April 2009	To clarify about non-investigational vaccines offered based on the preferences/recommendations of each participating country. To modify age related inclusion criteria.
04 February 2010	To clarify main analysis of the study and definition of the MITT (Modified Intention-To-Treat) Population.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/23324563