Clinical trial results:
A Phase 3, Open Label, Multi-Center, Extension Study to Assess Antibody Persistence and Response to a Third or Fifth Dose of Novartis Meningococcal B Recombinant Vaccine in 4-Year-Old Children Who Previously Participated in Study V72P12E1

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

Summary

EudraCT number	2011-004931-30
Trial protocol	GB ES IT CZ
Global end of trial date	09 April 2014

Results information

Result version number	v2 (current)
This version publication date	04 June 2016
First version publication date	19 December 2014
Version creation reason	• Correction of full data set re-QC sutdy needed because of EudraCT system glitch and updates to results are required.

Trial information

Trial identification

Sponsor protocol code	V72P12E2

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01717638
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)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	28 August 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	09 April 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main aim of the second extension study is to explore the bactericidal antibody persistence in 4-year-old children after a fourth dose boost of rMenB+OMV NZ given at 12, 18, or 24 months of age or after a two-dose catch-up schedule of rMenB+OMV NZ administered at either 12 and 14, 18 and 20, or 24 and 26 months of age in study V72P12E1.

Protection of trial subjects:

Standard immunization practices should be observed and care should be taken to administer the injection intramuscularly. As with all injectable vaccines, appropriate
medical treatment and supervision should be readily available in case of anaphylactic reactions following administration of the study vaccine, in accordance with local
practice/guidelines such as epinephrine 1:1000 and diphenhydramine.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 November 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 101
Country: Number of subjects enrolled	United Kingdom: 314
Country: Number of subjects enrolled	Czech Republic: 215
Country: Number of subjects enrolled	Italy: 175
Worldwide total number of subjects	805
EEA total number of subjects	805

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	805
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 from 4 centers in the UK; 4 centers in Italy; 4 centers in Spain; 19 centers in Czech Republic.

Pre-assignment

Screening details:

All enrolled subjects were included in the trial.

Period 1

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

Blinding implementation details:

The trial was designed as an open-label study; all subjects scheduled to receive vaccination received MenB vaccine (rMenB+OMV NZ). The personnel analyzing the serum at the centralized laboratory were blinded to the study group of the subject.

Arms

Are arms mutually exclusive?	Yes
Arm title	B+R246_12_48

Arm description:

Previously received rMenB+OMV NZ vaccine + routine vaccines at 2, 4 and 6 months of age followed by a booster dose of rMenB+OMV NZ vaccine at 12 months of age. One third of subjects from this group received a 5th dose of rMenB+OMV NZ vaccine in the present study at 4 years of age.

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

Dosage and administration details:

Subject received one injection of a 0.5 mL dose.

Arm title	B+R246_18_48

Arm description:

Previously received rMenB+OMV NZ vaccine + routine vaccines at 2, 4 and 6 months of age followed by a booster dose of rMenB+OMV NZ vaccine at 18 months of age. One third of subjects from this group received a 5th dose of rMenB+OMV NZ vaccine in the present study at 4 years of age.

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

Dosage and administration details:

Subject received one injection of a 0.5 mL dose.

Arm title	B+R246_24_48

Arm description:

Previously received rMenB+OMV NZ vaccine + routine vaccines at 2, 4 and 6 months of age followed by

a booster dose of rMenB+OMV NZ vaccine at 24 months of age. One third of subjects from this group received a 5th dose of rMenB+OMV NZ vaccine in the present study at 4 years of age.

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

Dosage and administration details:

Subject received one injection of a 0.5 mL dose.

Arm title	B246_12_48

Arm description:

Previously received 3 doses of rMenB+OMV NZ vaccine at 2, 4 and 6 months of age and routine vaccines at 3, 5 and 7 months of age, followed by a booster dose of rMenB+OMV NZ vaccine at 12 months of age. One third of subjects from this group received a 5th dose of rMenB+OMV NZ vaccine in the present study at 4 years of age.

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

Dosage and administration details:

Subject received one injection of a 0.5 mL dose.

Arm title	B246_18_48

Arm description:

Previously received 3 doses of rMenB+OMV NZ vaccine at 2, 4 and 6 months of age and routine vaccines at 3, 5 and 7 months of age, followed by a booster dose of rMenB+OMV NZ vaccine at 18 months of age. One third of subjects from this group received a 5th dose of rMenB+OMV NZ vaccine in the present study at 4 years of age.

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

Dosage and administration details:

Subject received one injection of a 0.5 mL dose.

Arm title	B246_24_48

Arm description:

Previously received 3 doses of rMenB+OMV NZ vaccine at 2, 4 and 6 months of age and routine vaccines at 3, 5 and 7 months of age, followed by a booster dose of rMenB+OMV NZ vaccine at 24 months of age. One third of subjects from this group received a 5th dose of rMenB+OMV NZ vaccine in the present study at 4 years of age.

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

Dosage and administration details:

Subject received one injection of a 0.5 mL dose.

Arm title	B+R234_12_48

Arm description:

Previously received rMenB+OMV NZ vaccine + routine vaccines at 2, 3 and 4 months of age followed by a booster dose of rMenB+OMV NZ vaccine at 12 months of age. All subjects received a 5th dose of rMenB+OMV NZ vaccine in the present study at 4 years of age.

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

Dosage and administration details:

Subject received one injection of a 0.5 mL dose.

Arm title	B+R234_18_48

Arm description:

Previously received rMenB+OMV NZ vaccine + routine vaccines at 2, 3 and 4 months of age followed by a booster dose of rMenB+OMV NZ vaccine at 18 months of age. All subjects received a 5th dose of rMenB+OMV NZ vaccine in the present study at 4 years of age.

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

Dosage and administration details:

Subject received one injection of a 0.5 mL dose.

Arm title	B+R234_24_48

Arm description:

Previously received rMenB+OMV NZ vaccine + routine vaccines at 2, 3 and 4 months of age followed by a booster dose of rMenB+OMV NZ vaccine at 24 months of age. All subjects received a 5th dose of rMenB+OMV NZ vaccine in the present study at 4 years of age.

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

Dosage and administration details:

Subject received one injection of a 0.5 mL dose.

Arm title	B12 14_48

Arm description:

Previously received two catch-up doses of rMenB+OMV NZ vaccine at 12 &14 months of age. All subjects received a 3rd dose of rMenB+OMV NZ vaccine in the present study at 4 years of age.

Arm type	Experimental

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

Dosage and administration details:

Subject received one injection of a 0.5 mL dose.

Arm title	B18 20_48

Arm description:

Previously received two catch-up doses of rMenB+OMV NZ vaccine at 18 & 20 months of age. All subjects from this group received a 3rd dose of rMenB+OMV NZ vaccine in the present study at 4 years of age.

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

Dosage and administration details:

Subject received one injection of a 0.5 mL dose.

Arm title	B24 26_48

Arm description:

Previously received two catch-up doses of rMenB+OMV NZ vaccine at 24 & 26 months of age. All subjects from this group received a 3rd dose of rMenB+OMV NZ vaccine in the present study at 4 years of age.

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

Dosage and administration details:

Subject received one injection of a 0.5 mL dose.

Arm title	B48 50

Arm description:

Newly recruited 4 year old naive subjects who received 2 catch-up doses of rMenB+OMV NZ vaccine, two months apart, in the present study.

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

Dosage and administration details:

Subject received one injection of a 0.5 mL dose.

Number of subjects in period 1	B+R246_12_48	B+R246_18_48	B+R246_24_48
Started	67	61	60
Completed	67	60	59
Not completed	0	1	1
Father in hospital	-	-	-
Consent withdrawn by subject	-	1	1
Lost to follow-up	-	-	-

Number of subjects in period 1	B246_12_48	B246_18_48	B246_24_48
Started	66	64	55
Completed	66	63	54
Not completed	0	1	1
Father in hospital	-	-	-
Consent withdrawn by subject	-	1	-
Lost to follow-up	-	-	1

Number of subjects in period 1	B+R234_12_48	B+R234_18_48	B+R234_24_48
Started	43	29	28
Completed	41	28	26
Not completed	2	1	2
Father in hospital	-	-	-
Consent withdrawn by subject	2	1	2
Lost to follow-up	-	-	-

Number of subjects in period 1	B12 14_48	B18 20_48	B24 26_48
Started	100	11	12
Completed	99	11	12
Not completed	1	0	0
Father in hospital	-	-	-
Consent withdrawn by subject	1	-	-
Lost to follow-up	-	-	-

Number of subjects in period 1	B48 50
Started	209
Completed	190
Not completed	19
Father in hospital	1
Consent withdrawn by subject	18
Lost to follow-up	-

Baseline characteristics

Reporting groups

Reporting group title	B+R246_12_48

Reporting group description:

Previously received rMenB+OMV NZ vaccine + routine vaccines at 2, 4 and 6 months of age followed by a booster dose of rMenB+OMV NZ vaccine at 12 months of age. One third of subjects from this group received a 5th dose of rMenB+OMV NZ vaccine in the present study at 4 years of age.

Reporting group title	B+R246_18_48

Reporting group description:

Previously received rMenB+OMV NZ vaccine + routine vaccines at 2, 4 and 6 months of age followed by a booster dose of rMenB+OMV NZ vaccine at 18 months of age. One third of subjects from this group received a 5th dose of rMenB+OMV NZ vaccine in the present study at 4 years of age.

Reporting group title	B+R246_24_48

Reporting group description:

Previously received rMenB+OMV NZ vaccine + routine vaccines at 2, 4 and 6 months of age followed by a booster dose of rMenB+OMV NZ vaccine at 24 months of age. One third of subjects from this group received a 5th dose of rMenB+OMV NZ vaccine in the present study at 4 years of age.

Reporting group title	B246_12_48

Reporting group description:

Previously received 3 doses of rMenB+OMV NZ vaccine at 2, 4 and 6 months of age and routine vaccines at 3, 5 and 7 months of age, followed by a booster dose of rMenB+OMV NZ vaccine at 12 months of age. One third of subjects from this group received a 5th dose of rMenB+OMV NZ vaccine in the present study at 4 years of age.

Reporting group title	B246_18_48

Reporting group description:

Previously received 3 doses of rMenB+OMV NZ vaccine at 2, 4 and 6 months of age and routine vaccines at 3, 5 and 7 months of age, followed by a booster dose of rMenB+OMV NZ vaccine at 18 months of age. One third of subjects from this group received a 5th dose of rMenB+OMV NZ vaccine in the present study at 4 years of age.

Reporting group title	B246_24_48

Reporting group description:

Previously received 3 doses of rMenB+OMV NZ vaccine at 2, 4 and 6 months of age and routine vaccines at 3, 5 and 7 months of age, followed by a booster dose of rMenB+OMV NZ vaccine at 24 months of age. One third of subjects from this group received a 5th dose of rMenB+OMV NZ vaccine in the present study at 4 years of age.

Reporting group title	B+R234_12_48

Reporting group description:

Previously received rMenB+OMV NZ vaccine + routine vaccines at 2, 3 and 4 months of age followed by a booster dose of rMenB+OMV NZ vaccine at 12 months of age. All subjects received a 5th dose of rMenB+OMV NZ vaccine in the present study at 4 years of age.

Reporting group title	B+R234_18_48

Reporting group description:

Previously received rMenB+OMV NZ vaccine + routine vaccines at 2, 3 and 4 months of age followed by a booster dose of rMenB+OMV NZ vaccine at 18 months of age. All subjects received a 5th dose of rMenB+OMV NZ vaccine in the present study at 4 years of age.

Reporting group title	B+R234_24_48

Reporting group description:

Previously received rMenB+OMV NZ vaccine + routine vaccines at 2, 3 and 4 months of age followed by a booster dose of rMenB+OMV NZ vaccine at 24 months of age. All subjects received a 5th dose of rMenB+OMV NZ vaccine in the present study at 4 years of age.

Reporting group title	B12 14_48

Reporting group description:

Previously received two catch-up doses of rMenB+OMV NZ vaccine at 12 &14 months of age. All subjects received a 3rd dose of rMenB+OMV NZ vaccine in the present study at 4 years of age.

Reporting group title	B18 20_48

Reporting group description:

Previously received two catch-up doses of rMenB+OMV NZ vaccine at 18 & 20 months of age. All subjects from this group received a 3rd dose of rMenB+OMV NZ vaccine in the present study at 4 years of age.

Reporting group title	B24 26_48

Reporting group description:

Previously received two catch-up doses of rMenB+OMV NZ vaccine at 24 & 26 months of age. All subjects from this group received a 3rd dose of rMenB+OMV NZ vaccine in the present study at 4 years of age.

Reporting group title	B48 50

Reporting group description:

Newly recruited 4 year old naive subjects who received 2 catch-up doses of rMenB+OMV NZ vaccine, two months apart, in the present study.

Reporting group values	B+R246_12_48	B+R246_18_48	B+R246_24_48
Number of subjects	67	61	60
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			
Analysis was done on the all enrolled population, ie, all subjects who have signed an informed consent, undergone screening procedure(s) and were randomized.			
Units: months			
arithmetic mean	51.8	52.1	51.7
standard deviation	± 3.4	± 3.4	± 3.5
Gender categorical			
Analysis was done on the all enrolled set.			
Units: Subjects			
Female	23	28	33
Male	44	33	27

Reporting group values	B246_12_48	B246_18_48	B246_24_48
Number of subjects	66	64	55

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			
Analysis was done on the all enrolled population, ie, all subjects who have signed an informed consent, undergone screening procedure(s) and were randomized.			
Units: months			
arithmetic mean	51.7	51.3	52.3
standard deviation	± 3.5	± 3.7	± 3.7
Gender categorical			
Analysis was done on the all enrolled set.			
Units: Subjects			
Female	28	32	30
Male	38	32	25

Reporting group values	B+R234_12_48	B+R234_18_48	B+R234_24_48
Number of subjects	43	29	28
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			
Analysis was done on the all enrolled population, ie, all subjects who have signed an informed consent, undergone screening procedure(s) and were randomized.			
Units: months			
arithmetic mean	51.8	51.4	53.1
standard deviation	± 3.4	± 3.4	± 3.5
Gender categorical			
Analysis was done on the all enrolled set.			
Units: Subjects			
Female	24	17	13
Male	19	12	15

Reporting group values	B12 14_48	B18 20_48	B24 26_48

Number of subjects	100	11	12
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			
Analysis was done on the all enrolled population, ie, all subjects who have signed an informed consent, undergone screening procedure(s) and were randomized.			
Units: months			
arithmetic mean	51.7	53.4	56.8
standard deviation	± 3.3	± 4.3	± 1.5
Gender categorical			
Analysis was done on the all enrolled set.			
Units: Subjects			
Female	50	6	4
Male	50	5	8

Reporting group values	B48 50	Total	
Number of subjects	209	805	
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			
Analysis was done on the all enrolled population, ie, all subjects who have signed an informed consent, undergone screening procedure(s) and were randomized.			
Units: months			
arithmetic mean	53.7		
standard deviation	± 3.6	-	
Gender categorical			
Analysis was done on the all enrolled set.			
Units: Subjects			
Female	99	387	
Male	110	418	

End points

End points reporting groups

Reporting group title	B+R246_12_48

Reporting group description:

Previously received rMenB+OMV NZ vaccine + routine vaccines at 2, 4 and 6 months of age followed by a booster dose of rMenB+OMV NZ vaccine at 12 months of age. One third of subjects from this group received a 5th dose of rMenB+OMV NZ vaccine in the present study at 4 years of age.

Reporting group title	B+R246_18_48

Reporting group description:

Previously received rMenB+OMV NZ vaccine + routine vaccines at 2, 4 and 6 months of age followed by a booster dose of rMenB+OMV NZ vaccine at 18 months of age. One third of subjects from this group received a 5th dose of rMenB+OMV NZ vaccine in the present study at 4 years of age.

Reporting group title	B+R246_24_48

Reporting group description:

Previously received rMenB+OMV NZ vaccine + routine vaccines at 2, 4 and 6 months of age followed by a booster dose of rMenB+OMV NZ vaccine at 24 months of age. One third of subjects from this group received a 5th dose of rMenB+OMV NZ vaccine in the present study at 4 years of age.

Reporting group title	B246_12_48

Reporting group description:

Previously received 3 doses of rMenB+OMV NZ vaccine at 2, 4 and 6 months of age and routine vaccines at 3, 5 and 7 months of age, followed by a booster dose of rMenB+OMV NZ vaccine at 12 months of age. One third of subjects from this group received a 5th dose of rMenB+OMV NZ vaccine in the present study at 4 years of age.

Reporting group title	B246_18_48

Reporting group description:

Previously received 3 doses of rMenB+OMV NZ vaccine at 2, 4 and 6 months of age and routine vaccines at 3, 5 and 7 months of age, followed by a booster dose of rMenB+OMV NZ vaccine at 18 months of age. One third of subjects from this group received a 5th dose of rMenB+OMV NZ vaccine in the present study at 4 years of age.

Reporting group title	B246_24_48

Reporting group description:

Previously received 3 doses of rMenB+OMV NZ vaccine at 2, 4 and 6 months of age and routine vaccines at 3, 5 and 7 months of age, followed by a booster dose of rMenB+OMV NZ vaccine at 24 months of age. One third of subjects from this group received a 5th dose of rMenB+OMV NZ vaccine in the present study at 4 years of age.

Reporting group title	B+R234_12_48

Reporting group description:

Previously received rMenB+OMV NZ vaccine + routine vaccines at 2, 3 and 4 months of age followed by a booster dose of rMenB+OMV NZ vaccine at 12 months of age. All subjects received a 5th dose of rMenB+OMV NZ vaccine in the present study at 4 years of age.

Reporting group title	B+R234_18_48

Reporting group description:

Previously received rMenB+OMV NZ vaccine + routine vaccines at 2, 3 and 4 months of age followed by a booster dose of rMenB+OMV NZ vaccine at 18 months of age. All subjects received a 5th dose of rMenB+OMV NZ vaccine in the present study at 4 years of age.

Reporting group title	B+R234_24_48

Reporting group description:

Previously received rMenB+OMV NZ vaccine + routine vaccines at 2, 3 and 4 months of age followed by a booster dose of rMenB+OMV NZ vaccine at 24 months of age. All subjects received a 5th dose of rMenB+OMV NZ vaccine in the present study at 4 years of age.

Reporting group title	B12 14_48

Reporting group description:

Previously received two catch-up doses of rMenB+OMV NZ vaccine at 12 &14 months of age. All subjects received a 3rd dose of rMenB+OMV NZ vaccine in the present study at 4 years of age.

Reporting group title	B18 20_48

Reporting group description:

Previously received two catch-up doses of rMenB+OMV NZ vaccine at 18 & 20 months of age. All subjects from this group received a 3rd dose of rMenB+OMV NZ vaccine in the present study at 4 years of age.

Reporting group title	B24 26_48

Reporting group description:

Previously received two catch-up doses of rMenB+OMV NZ vaccine at 24 & 26 months of age. All subjects from this group received a 3rd dose of rMenB+OMV NZ vaccine in the present study at 4 years of age.

Reporting group title	B48 50

Reporting group description:

Newly recruited 4 year old naive subjects who received 2 catch-up doses of rMenB+OMV NZ vaccine, two months apart, in the present study.

Primary: 1) Percentages of Subjects With Persisting Serum Bactericidal Titers ≥1:5 and ≥1:8 (at 4 Years of Age), Who Had Previously Received Three Primary Doses and One Booster Dose of rMenB+OMV NZ Vaccine According to Different Schedules

End point title	1) Percentages of Subjects With Persisting Serum Bactericidal Titers ≥1:5 and ≥1:8 (at 4 Years of Age), Who Had Previously Received Three Primary Doses and One Booster Dose of rMenB+OMV NZ Vaccine According to Different Schedules[1][2]

End point description:

The antibody persistence at 4 years of age in children who had previously received 3 primary doses (at 2, 3, 4, or 2, 4, 6 months) followed by a booster dose (at 12,18 or 24 months) of rMenB+OMV NZ vaccine according to different schedules is compared with the response in naïve children and reported as percentages of subjects with human serum bactericidal assay (hSBA) titers ≥1:5 and ≥1:8.

Analysis was done on the Full Analysis set (FAS), Persistence, ie, all subjects in the enrolled population who provided at least one evaluable serum sample at baseline (visit 1).

End point type	Primary

End point timeframe:

Day 1 (24-36 months post booster; baseline for naive)

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: No statistical analysis is associated to this endpoint.

[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: No statistical analysis is associated to this endpoint.

End point values	B+R246_12_48	B+R246_18_48	B+R246_24_48	B246_12_48
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	67	60	60	66
Units: Percentages of Subjects				
number (confidence interval 95%)				
H44/76 - ≥1:5; N=67,60,59,65,63,54,42,28,28,206	12 (5 to 22)	18 (10 to 30)	24 (14 to 37)	20 (11 to 32)

5/99 - ≥1:5; N=67,60,58,64,62,54,42,28,28,200	93 (83 to 98)	98 (91 to 100)	97 (88 to 100)	97 (89 to 100)
NZ 98/254 - ≥ 1:5	9 (3 to 18)	8 (3 to 18)	12 (5 to 23)	9 (3 to 19)
M10713 - ≥1:5; N=65,59,58,62,60,54,40,28,28,192	54 (41 to 66)	68 (54 to 79)	74 (61 to 85)	55 (42 to 68)
H44/76-≥1:8; N=67,60,59,65,63,54,42,28,28,206	7 (2 to 17)	10 (4 to 21)	17 (8 to 29)	11 (4 to 21)
5/99 - ≥1:8; N=67,60,58,64,62,54,42,28,28,200	91 (82 to 97)	97 (88 to 100)	93 (83 to 98)	94 (85 to 98)
NZ 98/254 - ≥ 1:8	4 (1 to 13)	5 (1 to 14)	8 (3 to 18)	8 (3 to 17)
M10713 - ≥1:8; N=65,59,58,62,60,54,40,28,28,192	49 (37 to 62)	53 (39 to 66)	60 (47 to 73)	48 (35 to 61)

End point values	B246_18_48	B246_24_48	B+R234_12_48	B+R234_18_48
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	63	54	42	28
Units: Percentages of Subjects				
number (confidence interval 95%)				
H44/76 - ≥1:5; N=67,60,59,65,63,54,42,28,28,206	27 (17 to 40)	35 (23 to 49)	12 (4 to 26)	25 (11 to 45)
5/99 - ≥1:5; N=67,60,58,64,62,54,42,28,28,200	100 (94 to 100)	100 (93 to 100)	90 (77 to 97)	89 (72 to 98)
NZ 98/254 - ≥ 1:5	11 (5 to 22)	9 (3 to 20)	10 (3 to 23)	11 (2 to 28)
M10713 - ≥1:5; N=65,59,58,62,60,54,40,28,28,192	53 (40 to 66)	80 (66 to 89)	68 (51 to 81)	75 (55 to 89)
H44/76-≥1:8; N=67,60,59,65,63,54,42,28,28,206	24 (14 to 36)	28 (16 to 42)	7 (1 to 19)	21 (8 to 41)
5/99 - ≥1:8; N=67,60,58,64,62,54,42,28,28,200	94 (84 to 98)	100 (93 to 100)	90 (77 to 97)	86 (67 to 97)
NZ 98/254 - ≥ 1:8	3 (0 to 11)	4 (0 to 13)	2 (0.06 to 13)	7 (1 to 24)
M10713 - ≥1:8; N=65,59,58,62,60,54,40,28,28,192	45 (32 to 58)	65 (51 to 77)	60 (43 to 75)	61 (41 to 78)

End point values	B+R234_24_48	B48 50		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	206		
Units: Percentages of Subjects				
number (confidence interval 95%)				
H44/76 - ≥1:5; N=67,60,59,65,63,54,42,28,28,206	21 (8 to 41)	0 (0 to 3)		
5/99 - ≥1:5; N=67,60,58,64,62,54,42,28,28,200	96 (82 to 100)	5 (2 to 8)		
NZ 98/254 - ≥ 1:5	11 (2 to 28)	0 (0 to 3)		
M10713 - ≥1:5; N=65,59,58,62,60,54,40,28,28,192	75 (55 to 89)	60 (53 to 67)		
H44/76-≥1:8; N=67,60,59,65,63,54,42,28,28,206	21 (8 to 41)	0 (0 to 3)		
5/99 - ≥1:8; N=67,60,58,64,62,54,42,28,28,200	96 (82 to 100)	3 (1 to 6)		
NZ 98/254 - ≥ 1:8	11 (2 to 28)	0 (0 to 3)		

M10713 - ≥1:8; N=65,59,58,62,60,54,40,28,28,192	61 (41 to 78)	56 (48 to 63)		

Statistical analyses

No statistical analyses for this end point

Primary: 2) Persisting antibody titers in children (at 4 years of age), who had previously received three primary doses and one booster dose of rMenB+OMV NZ vaccine according to different schedules.

End point title	2) Persisting antibody titers in children (at 4 years of age), who had previously received three primary doses and one booster dose of rMenB+OMV NZ vaccine according to different schedules.[3][4]

End point description:

The persisting antibody titers at 4 years of age in children who had previously received 3 primary doses (at 2, 3, 4,or 2, 4, 6 months) followed by a booster dose (at 12, 18 or 24 months) of rMenB+OMV NZ vaccine according to different schedules is compared with the titers in naive children and reported as geometric mean titers (GMTs).

Analysis was done on FAS (Persistence).

End point type	Primary

End point timeframe:

Day 1 (24-36 months post booster; baseline for naive)

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis is associated to this endpoint.

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis is associated to this endpoint.

End point values	B+R246_12_48	B+R246_18_48	B+R246_24_48	B246_12_48
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	67	60	60	66
Units: Titers				
geometric mean (confidence interval 95%)				
H44/76; N=67,60,59,65,63,54,42,28,28,206	1.75 (1.36 to 2.25)	1.68 (1.29 to 2.19)	2.41 (1.83 to 3.19)	1.72 (1.29 to 2.29)
5/99; N=67,60,58,64,62,54,42,28,28,200	36 (27 to 48)	69 (50 to 94)	69 (50 to 96)	59 (45 to 78)
NZ 98/254	1.25 (1.03 to 1.52)	1.29 (1.05 to 1.59)	1.38 (1.11 to 1.72)	1.48 (1.2 to 1.83)
M10713; N=65,59,58,62,60,54,40,28,28,192	6.14 (4.19 to 8.99)	7.36 (4.94 to 11)	9.08 (5.97 to 14)	7.86 (5.17 to 12)

End point values	B246_18_48	B246_24_48	B+R234_12_48	B+R234_18_48

Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	63	54	42	28
Units: Titers				
geometric mean (confidence interval 95%)				
H44/76; N=67,60,59,65,63,54,42,28,28,206	1.99 (1.49 to 2.65)	2.69 (1.96 to 3.7)	1.51 (1.04 to 2.18)	2.2 (1.38 to 3.49)
5/99; N=67,60,58,64,62,54,42,28,28,200	57 (43 to 75)	111 (82 to 151)	52 (34 to 81)	62 (36 to 108)
NZ 98/254	1.34 (1.08 to 1.66)	1.52 (1.2 to 1.92)	1.32 (1.05 to 1.65)	1.25 (0.94 to 1.66)
M10713; N=65,59,58,62,60,54,40,28,28,192	7.77 (5.07 to 12)	15 (9.49 to 24)	9.61 (5.81 to 16)	11 (5.92 to 20)

End point values	B+R234_24_48	B48 50		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	206		
Units: Titers				
geometric mean (confidence interval 95%)				
H44/76; N=67,60,59,65,63,54,42,28,28,206	2.2 (1.37 to 3.53)	1.04 (1.01 to 1.07)		
5/99; N=67,60,58,64,62,54,42,28,28,200	101 (57 to 177)	1.15 (1.05 to 1.27)		
NZ 98/254	1.62 (1.21 to 2.16)	1.01 (0.99 to 1.03)		
M10713; N=65,59,58,62,60,54,40,28,28,192	11 (5.9 to 21)	8.75 (6.74 to 11)		

Statistical analyses

No statistical analyses for this end point

Primary: 3) Geometric mean ratio (GMR) in children (at 4 years of age) who had previously received three primary doses at 2, 4, 6 months of age and one booster dose of rMenB+OMV NZ vaccine according to different schedules

End point title	3) Geometric mean ratio (GMR) in children (at 4 years of age) who had previously received three primary doses at 2, 4, 6 months of age and one booster dose of rMenB+OMV NZ vaccine according to different schedules[5][6]

End point description:

The geometric mean ratio (GMR) of GMTs (48 months/one month post booster vaccination) at 4 years of age in children who had previously received 3 primary doses at 2, 4, 6 months of age followed by a booster dose (at 12,18 or 24 months) of rMenB+OMV NZ vaccine according to different schedules is reported.
GMTs against M10713 strain were not calculated for these groups in the parent study therefore the ratios cannot be available.
Analysis was done on FAS (Persistence).

End point type	Primary

End point timeframe:

Day 1 (24-36 months post booster dose; baseline for naive)

Notes:

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

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis is associated to this endpoint.

End point values	B+R246_12_48	B+R246_18_48	B+R246_24_48	B246_12_48
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	63	57	54	59
Units: Ratio				
geometric mean (confidence interval 95%)				
H44/76; N=62,56,52,57,55,46,38,27,25,206	0.012 (0.0091 to 0.017)	0.013 (0.0096 to 0.018)	0.023 (0.016 to 0.033)	0.0092 (0.0066 to 0.013)
5/99; N=61,57,50,57,55,44,37,27,25,200	0.029 (0.023 to 0.037)	0.032 (0.026 to 0.041)	0.043 (0.033 to 0.056)	0.031 (0.024 to 0.041)
NZ 98/254	0.028 (0.021 to 0.039)	0.094 (0.067 to 0.13)	0.071 (0.05 to 0.1)	0.043 (0.031 to 0.06)

End point values	B246_18_48	B246_24_48		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	47		
Units: Ratio				
geometric mean (confidence interval 95%)				
H44/76; N=62,56,52,57,55,46,38,27,25,206	0.013 (0.0097 to 0.018)	0.023 (0.016 to 0.033)		
5/99; N=61,57,50,57,55,44,37,27,25,200	0.034 (0.026 to 0.045)	0.054 (0.04 to 0.074)		
NZ 98/254	0.081 (0.058 to 0.11)	0.11 (0.075 to 0.16)		

Statistical analyses

No statistical analyses for this end point

Primary: 26) Geometric Mean Ratios (GMRs) in Children (at 4 Years of Age) Who Had Previously Received Three Primary Doses at 2, 3, 4 months of age and One Booster Dose of rMenB+OMV NZ Vaccine According to Different Schedules

End point title	26) Geometric Mean Ratios (GMRs) in Children (at 4 Years of Age) Who Had Previously Received Three Primary Doses at 2, 3, 4 months of age and One Booster Dose of rMenB+OMV NZ Vaccine According to Different Schedules[7][8]

End point description:

The GMRs of GMTs (48 months/one month post booster vaccination) at 4 years of age in children who had previously received 3 primary doses at 2, 3, 4 months of age followed by a booster dose (at 12,18 or 24 months) of rMenB+OMV NZ vaccine according to different schedules is reported.
Analysis was done on FAS (Persistence).

End point type	Primary

End point timeframe:

Day 1 (24-36 months post booster dose; baseline for naive)

Notes:

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

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis is associated to this endpoint.

End point values	B+R234_12_48	B+R234_18_48	B+R234_24_48	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	39	28	25	
Units: Ratio				
geometric mean (confidence interval 95%)				
H44/76; N=38,27,25	0.0091 (0.0064 to 0.013)	0.023 (0.015 to 0.036)	0.023 (0.014 to 0.036)	
5/99; N=37,27,25	0.035 (0.026 to 0.048)	0.037 (0.025 to 0.054)	0.055 (0.037 to 0.081)	
NZ 98/254	0.03 (0.02 to 0.044)	0.082 (0.05 to 0.14)	0.066 (0.038 to 0.11)	
M10713; N=26,24,25	0.67 (0.32 to 1.4)	0.91 (0.4 to 2.05)	0.47 (0.21 to 1.07)	

Statistical analyses

No statistical analyses for this end point

Secondary: 4) Percentages of subjects with persisting serum bactericidal titers ≥1:5 and ≥1:8 (at 4 years of age), who had previously received two catch up doses of rMenB+OMV NZ vaccine according to different schedules

End point title	4) Percentages of subjects with persisting serum bactericidal titers ≥1:5 and ≥1:8 (at 4 years of age), who had previously received two catch up doses of rMenB+OMV NZ vaccine according to different schedules[9]

End point description:

The antibody persistence in children at 4 year of age, who had previously received 2 catch up doses (at 12, 14 or 18, 20 or 24, 26 months) according to different schedules is reported as number of subjects with hSBA titers ≥1:5 and hSBA titers ≥1:8.

Analysis was done on FAS (Persistence).

End point type	Secondary

End point timeframe:

Day 1 (22-34 months post last MenB vaccine)

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: No statistical analysis is associated to this endpoint.

End point values	B12 14_48	B18 20_48	B24 26_48	B48 50
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	96	11	11	206
Units: Percentages of subjects				
number (confidence interval 95%)				
hSBA≥ 1:5 (H44/76 strain)	11 (6 to 20)	9 (0 to 41)	9 (0 to 41)	0 (0 to 3)
hSBA≥ 1:5 (5/99 strain; N=96,11,11,200)	84 (76 to 91)	100 (72 to 100)	100 (72 to 100)	5 (2 to 8)
hSBA≥ 1:5 (NZ 98/254 strain)	3 (1 to 9)	18 (2 to 52)	0 (0 to 28)	0 (0 to 3)
hSBA≥ 1:5 (M10713 strain; N=96,10,10,192)	59 (49 to 69)	60 (26 to 88)	60 (26 to 88)	60 (53 to 67)
hSBA≥ 1:8 (H44/76 strain)	8 (4 to 16)	9 (0 to 41)	0 (0 to 28)	0 (0 to 3)
hSBA≥ 1:8 (5/99 strain; N=96,11,11,200)	81 (72 to 88)	100 (72 to 100)	100 (72 to 100)	3 (1 to 6)
hSBA≥ 1:8 (NZ 98/254 strain)	2 (0 to 7)	18 (2 to 52)	0 (0 to 28)	0 (0 to 3)
hSBA≥ 1:8 (M10713 strain; N=96,10,10,192)	49 (39 to 59)	40 (12 to 74)	60 (26 to 88)	56 (48 to 63)

Statistical analyses

No statistical analyses for this end point

Secondary: 5) Persisting antibody titers in children (at 4 years of age) who had previously received two catch up doses of rMenB+OMV NZ vaccine according to different schedules

End point title	5) Persisting antibody titers in children (at 4 years of age) who had previously received two catch up doses of rMenB+OMV NZ vaccine according to different schedules[10]

End point description:

The persisting GMTs in children at 4 years of age, who had previously received 2 catch up doses (at 12, 14 or 18, 20 or 24, 26 months) of rMenB+OMV NZ vaccine according to different schedules are reported.

Analysis was done on FAS (Persistence).

End point type	Secondary

End point timeframe:

Day 1 (22-36 months post last MenB vaccine; baseline for naive)

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: No statistical analysis is associated to this endpoint.

End point values	B12 14_48	B18 20_48	B24 26_48	B48 50
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	96	11	11	206
Units: Titers				
geometric mean (confidence interval 95%)				
H44/76 strain	1.61 (1.3 to 2)	2.03 (1.11 to 3.72)	1.69 (0.91 to 3.12)	1.04 (1.01 to 1.07)
5/99 strain; N=96, 11, 11, 200	23 (17 to 32)	47 (20 to 112)	69 (29 to 165)	1.15 (1.05 to 1.27)

NZ 98/254 strain	1.15 (0.96 to 1.37)	2.68 (1.65 to 4.36)	1.06 (0.65 to 1.75)	1.01 (0.99 to 1.03)
M10713 strain; N=96, 10, 10, 192	7.83 (5.54 to 11)	9.67 (3.54 to 26)	8.4 (3.03 to 23)	8.75 (6.74 to 11)

Statistical analyses

No statistical analyses for this end point

Secondary: 6) GMRs of GMTs in children (at 4 years of age) who had previously received two catch up doses of rMenB+OMV NZ vaccine according to different schedules

End point title	6) GMRs of GMTs in children (at 4 years of age) who had previously received two catch up doses of rMenB+OMV NZ vaccine according to different schedules[11]

End point description:

The GMRs af GMTs (48 months/one month post last vaccination) in children at 4 years of age who had previously received 2 catch up doses (at 12, 14 or 18, 20 or 24, 26 months) of rMenB+OMV NZ vaccine according to different schedules. Analysis was done on FAS (Persistence).

End point type	Secondary

End point timeframe:

Day 1 (22-36 months post last MenB vaccine)

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis is associated to this endpoint.

End point values	B12 14_48	B18 20_48	B24 26_48	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	88	9	10	
Units: Ratio				
geometric mean (confidence interval 95%)				
H44/76 strain	0.092 (0.069 to 0.12)	0.18 (0.078 to 0.43)	0.2 (0.086 to 0.45)	
5/99 strain	0.45 (0.34 to 0.59)	1.9 (0.84 to 4.29)	1.36 (0.62 to 3)	
NZ 98/254 strain; N=88, 9, 8	0.28 (0.21 to 0.37)	0.73 (0.32 to 1.68)	0.42 (0.17 to 1.01)	
M10713 strain; N=7, 7, 8	11 (3.34 to 38)	6.05 (1.45 to 25)	6.88 (1.68 to 28)	

Statistical analyses

No statistical analyses for this end point

Secondary: 7) Percentages of subjects with hSBA titers ≥1:5 and ≥1:8 after a 5th dose of rMenB+OMV NZ vaccine (at 4 years of age) administered to children who had previously received 3 primary doses and a booster dose of the same vaccine

End point title	7) Percentages of subjects with hSBA titers ≥1:5 and ≥1:8 after a 5th dose of rMenB+OMV NZ vaccine (at 4 years of age) administered to children who had previously received 3 primary doses and a booster dose of the same vaccine[12]

End point description:

The percentages of subjects with hSBA titers ≥1:5 and ≥1:8, one month after a 5th dose of rMenB+OMV NZ vaccine was given children who had previously received 3 primary doses (at 2, 3, 4,or 2, 4, 6 months) and a booster dose (at 12, 18 or 24 months) of the same vaccine according to different schedules is compared with the hSBA response of children who received first dose of rMenB+OMV NZ at 4 years of age.

Analysis was done on FAS, Immunogenicity, ie, all subjects in the enrolled population who actually received a study vaccination, and provided at least one evaluable serum sample at post baseline.

End point type	Secondary

End point timeframe:

Day 31 (1 month post 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: No statistical analysis is associated to this endpoint.

End point values	B+R246_12_48	B+R246_18_48	B+R246_24_48	B246_12_48
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	26	18	16	16
Units: Percentages of subjects				
geometric mean (confidence interval 95%)				
H44/76 - ≥1:5; N=26,18,16,16,26,15,39,26,26,175	100 (87 to 100)	100 (81 to 100)	100 (79 to 100)	100 (79 to 100)
5/99 - ≥1:5; N=26,18,16,16,26,15,38,26,26,171	100 (87 to 100)	100 (81 to 100)	100 (79 to 100)	100 (79 to 100)
NZ 98/254 - ≥1:5; N=26,18,16,16,26,15,40,26,26,173	92 (75 to 99)	83 (59 to 96)	94 (70 to 100)	81 (54 to 96)
M10713 - ≥1:5; N=25,18,16,14,25,15,36,25,25,167	84 (64 to 95)	89 (65 to 99)	88 (62 to 98)	93 (66 to 100)
H44/76 - ≥1:8; N=26,18,16,16,26,15,39,26,26,175	96 (80 to 100)	100 (81 to 100)	100 (79 to 100)	100 (79 to 100)
5/99 - ≥1:8; N=26,18,16,16,26,15,38,26,26,171	100 (87 to 100)	100 (81 to 100)	100 (79 to 100)	100 (79 to 100)
NZ 98/254 - ≥1:8; N=26,18,16,16,26,15,40,26,26,173	85 (65 to 96)	61 (36 to 83)	81 (54 to 96)	75 (48 to 93)
M10713 - ≥1:8; N=25,18,16,14,25,15,36,25,25,167	76 (55 to 91)	89 (65 to 99)	88 (62 to 98)	93 (66 to 100)

End point values	B246_18_48	B246_24_48	B+R234_12_48	B+R234_18_48
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	26	15	40	26
Units: Percentages of subjects				
geometric mean (confidence interval 95%)				
H44/76 - ≥1:5; N=26,18,16,16,26,15,39,26,26,175	100 (87 to 100)	100 (78 to 100)	97 (87 to 100)	100 (87 to 100)
5/99 - ≥1:5; N=26,18,16,16,26,15,38,26,26,171	88 (70 to 98)	100 (78 to 100)	100 (91 to 100)	100 (87 to 100)

NZ 98/254 - ≥1:5; N=26,18,16,16,26,15,40,26,26,173	88 (70 to 98)	80 (52 to 96)	95 (83 to 99)	92 (75 to 99)
M10713 - ≥1:5; N=25,18,16,14,25,15,36,25,25,167	96 (80 to 100)	93 (68 to 100)	97 (85 to 100)	100 (86 to 100)
H44/76 - ≥1:8; N=26,18,16,16,26,15,39,26,26,175	96 (80 to 100)	100 (78 to 100)	97 (87 to 100)	100 (87 to 100)
5/99 - ≥1:8; N=26,18,16,16,26,15,38,26,26,171	100 (87 to 100)	100 (78 to 100)	100 (91 to 100)	100 (87 to 100)
NZ 98/254 - ≥1:8; N=26,18,16,16,26,15,40,26,26,173	88 (70 to 98)	80 (52 to 96)	88 (73 to 96)	81 (61 to 93)
M10713 - ≥1:8; N=25,18,16,14,25,15,36,25,25,167	96 (80 to 100)	93 (68 to 100)	97 (85 to 100)	100 (86 to 100)

End point values	B+R234_24_48	B48 50		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	175		
Units: Percentages of subjects				
geometric mean (confidence interval 95%)				
H44/76 - ≥1:5; N=26,18,16,16,26,15,39,26,26,175	100 (87 to 100)	71 (64 to 78)		
5/99 - ≥1:5; N=26,18,16,16,26,15,38,26,26,171	100 (87 to 100)	90 (85 to 94)		
NZ 98/254 - ≥1:5; N=26,18,16,16,26,15,40,26,26,173	92 (75 to 99)	24 (18 to 31)		
M10713 - ≥1:5; N=25,18,16,14,25,15,36,25,25,167	100 (86 to 100)	77 (70 to 83)		
H44/76 - ≥1:8; N=26,18,16,16,26,15,39,26,26,175	96 (80 to 100)	63 (55 to 70)		
5/99 - ≥1:8; N=26,18,16,16,26,15,38,26,26,171	100 (87 to 100)	87 (81 to 92)		
NZ 98/254 - ≥1:8; N=26,18,16,16,26,15,40,26,26,173	88 (70 to 98)	17 (12 to 24)		
M10713 - ≥1:8; N=25,18,16,14,25,15,36,25,25,167	96 (80 to 100)	74 (67 to 81)		

Statistical analyses

No statistical analyses for this end point

Secondary: 8) GMTs following a fifth dose of rMenB+OMV NZ vaccine (at 4 years of age) in children who had previously received 3 primary doses and a booster dose of the same vaccine according to different schedules

End point title	8) GMTs following a fifth dose of rMenB+OMV NZ vaccine (at 4 years of age) in children who had previously received 3 primary doses and a booster dose of the same vaccine according to different schedules[13]

End point description:

The GMTs, at one month after a 5th dose of rMenB+OMV NZ vaccine in children who had previously received 3 primary doses (at 2, 3, 4,or 2, 4, 6 months) and a booster dose (at 12, 18 or 24 months) of rMenB+OMV NZ vaccine according to different schedules, are compared with the GMTs of children who received first dose of rMenB+OMV NZ at 4 years of age.

Analysis was done on FAS (Immunogenicity).

End point type	Secondary

End point timeframe:

Day 31 (1 month post vaccination)

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: No statistical analysis is associated to this endpoint.

End point values	B+R246_12_48	B+R246_18_48	B+R246_24_48	B246_12_48
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	26	18	16	16
Units: Titers				
geometric mean (confidence interval 95%)				
H44/76 strain; N=26,18,16,16,26,15,39,26,26,175	108 (70 to 168)	115 (68 to 195)	107 (61 to 188)	173 (98 to 303)
5/99 strain; N=26,18,16,16,26,15,38,26,26,171	754 (478 to 1190)	1719 (993 to 2976)	933 (518 to 1682)	1959 (1091 to 3517)
NZ 98/254 strain; N=26,18,16,16,26,15,40,26,26,173	22 (13 to 36)	11 (5.66 to 20)	28 (14 to 55)	16 (8.2 to 31)
M10713 strain; N=25,18,16,14,25,15,36,25,25,167	22 (13 to 37)	19 (10 to 36)	28 (14 to 54)	32 (16 to 65)

End point values	B246_18_48	B246_24_48	B+R234_12_48	B+R234_18_48
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	26	15	40	26
Units: Titers				
geometric mean (confidence interval 95%)				
H44/76 strain; N=26,18,16,16,26,15,39,26,26,175	191 (123 to 297)	212 (199 to 379)	167 (109 to 258)	146 (85 to 251)
5/99 strain; N=26,18,16,16,26,15,38,26,26,171	1387 (878 to 2191)	1954 (1068 to 3575)	1711 (1186 to 2470)	1239 (787 to 1953)
NZ 98/254 strain; N=26,18,16,16,26,15,40,26,26,173	21 (13 to 36)	15 (7.66 to 31)	26 (18 to 36)	18 (12 to 28)
M10713 strain; N=25,18,16,14,25,15,36,25,25,167	37 (22 to 63)	33 (17 to 64)	53 (40 to 71)	58 (40 to 84)

End point values	B+R234_24_48	B48 50		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	175		
Units: Titers				
geometric mean (confidence interval 95%)				
H44/76 strain; N=26,18,16,16,26,15,39,26,26,175	135 (78 to 235)	11 (8.51 to 14)		

5/99 strain; N=26,18,16,16,26,15,38,26,26,171	1280 (803 to 2041)	34 (27 to 42)		
NZ 98/254 strain; N=26,18,16,16,26,15,40,26,26,173	27 (18 to 42)	2.25 (1.84 to 2.75)		
M10713 strain; N=25,18,16,14,25,15,36,25,25,167	51 (35 to 73)	20 (15 to 25)		

Statistical analyses

No statistical analyses for this end point

Secondary: 9) GMRs of GMTs following a fifth dose of rMenB+OMV NZ vaccine (at 4 years of age), in children who had previously received 3 primary doses and a booster dose of the same vaccine according to different schedules

End point title	9) GMRs of GMTs following a fifth dose of rMenB+OMV NZ vaccine (at 4 years of age), in children who had previously received 3 primary doses and a booster dose of the same vaccine according to different schedules[14]

End point description:

The GMRs of GMTs (one month post booster/48 months persistence), one month after a 5th dose of rMenB+OMV NZ vaccine in children who had previously received 3 primary doses (at 2, 3, 4,or 2, 4, 6 months) and a booster dose (at 12, 18 or 24 months) of rMenB+OMV NZ vaccine according to different schedules, are compared with the GMR (one month post 1 dose\baseline) of children who received first dose of rMenB+OMV NZ at 4 years of age.

Analysis was done on FAS (Immunogenicity).

End point type	Secondary

End point timeframe:

Day 31 (1 month post vaccination)

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: No statistical analysis is associated to this endpoint.

End point values	B+R246_12_48	B+R246_18_48	B+R246_24_48	B246_12_48
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	26	18	16	16
Units: Ratio				
geometric mean (confidence interval 95%)				
H44/76 strain; N=26,18,16,16,26,15,39,25,26,175	60 (40 to 92)	72 (44 to 120)	41 (24 to 71)	77 (45 to 132)
5/99 strain; N=26,18,16,15,25,15,38,25,26,168	32 (22 to 47)	23 (15 to 36)	15 (9.45 to 25)	30 (18 to 49)
NZ 98/254 strain; N=26,18,16,16,26,15,40,25,26,173	17 (10 to 29)	10 (5.43 to 19)	19 (9.54 to 37)	8.93 (4.75 to 17)
M10713 strain; N=24,17,16,12,23,15,35,24,25,158	3.15 (1.81 to 5.48)	4.46 (2.31 to 8.6)	3.36 (1.69 to 6.7)	3.49 (1.58 to 7.7)

End point values	B246_18_48	B246_24_48	B+R234_12_48	B+R234_18_48

Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	26	15	40	25
Units: Ratio				
geometric mean (confidence interval 95%)				
H44/76 strain; N=26,18,16,16,26,15,39,25,26,175	88 (58 to 134)	46 (26 to 80)	109 (71 to 167)	63 (37 to 108)
5/99 strain; N=26,18,16,15,25,15,38,25,26,168	20 (13 to 29)	18 (11 to 29)	33 (23 to 49)	20 (12 to 32)
NZ 98/254 strain; N=26,18,16,16,26,15,40,25,26,173	17 (10 to 29)	13 (6.48 to 26)	19 (14 to 27)	14 (9.35 to 22)
M10713 strain; N=24,17,16,12,23,15,35,24,25,158	3.74 (2.12 to 6.59)	4.21 (2.08 to 8.51)	5.35 (3.48 to 8.21)	3.86 (2.23 to 6.66)

End point values	B+R234_24_48	B48 50		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	175		
Units: Ratio				
geometric mean (confidence interval 95%)				
H44/76 strain; N=26,18,16,16,26,15,39,25,26,175	64 (37 to 110)	10 (8.2 to 13)		
5/99 strain; N=26,18,16,15,25,15,38,25,26,168	12 (7.16 to 19)	29 (23 to 37)		
NZ 98/254 strain; N=26,18,16,16,26,15,40,25,26,173	17 (11 to 26)	2.25 (1.84 to 2.75)		
M10713 strain; N=24,17,16,12,23,15,35,24,25,158	4.04 (2.35 to 6.94)	2 (1.62 to 2.46)		

Statistical analyses

No statistical analyses for this end point

Secondary: 10) Percentages of subjects with fourfold increase in hSBA titers after a 5th dose of rMenB+OMV NZ (at 4 years of age) was administered to children who previously received 3 primary and a booster dose of the same vaccine according to different schedules

End point title	10) Percentages of subjects with fourfold increase in hSBA titers after a 5th dose of rMenB+OMV NZ (at 4 years of age) was administered to children who previously received 3 primary and a booster dose of the same vaccine according to different schedules[15]

End point description:

The fourfold increase in hSBA titers, one month after a 5th dose of rMenB+OMV NZ vaccine was given to children who had previously received 3 primary doses (at 2, 3, 4,or 2, 4, 6 months) and a booster dose (at 12, 18 or 24 months) of rMenB+OMV NZ vaccine according to different schedules, is compared with the response in children who received the first dose of rMenB+OMV NZ vaccine at 4 years of age.

Analysis was done on FAS, Immunogenicity.

End point type	Secondary

End point timeframe:

Day 31 (1 month post vaccination)

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: No statistical analysis is associated to this endpoint.

End point values	B+R246_12_48	B+R246_18_48	B+R246_24_48	B246_12_48
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	26	18	16	16
Units: Percentages of subjects				
number (confidence interval 95%)				
H44/76 strain; N=26,18,16,16,26,15,39,25,26,175	92 (75 to 99)	100 (81 to 100)	100 (79 to 100)	100 (79 to 100)
5/99 strain; N=26,18,16,15,25,15,38,25,26,168	96 (80 to 100)	94 (73 to 100)	94 (70 to 100)	100 (78 to 100)
NZ 98/254 strain; N=26,18,16,16,26,15,40,25,26,173	81 (61 to 93)	61 (36 to 83)	81 (54 to 96)	69 (41 to 89)
M10713 strain; N=24,17,16,12,23,15,35,24,25,158	38 (19 to 59)	47 (23 to 72)	31 (11 to 59)	33 (10 to 65)

End point values	B246_18_48	B246_24_48	B+R234_12_48	B+R234_18_48
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	26	15	40	25
Units: Percentages of subjects				
number (confidence interval 95%)				
H44/76 strain; N=26,18,16,16,26,15,39,25,26,175	96 (80 to 100)	93 (68 to 100)	97 (87 to 100)	96 (80 to 100)
5/99 strain; N=26,18,16,15,25,15,38,25,26,168	92 (74 to 99)	100 (78 to 100)	97 (86 to 100)	96 (80 to 100)
NZ 98/254 strain; N=26,18,16,16,26,15,40,25,26,173	88 (70 to 98)	73 (45 to 92)	88 (73 to 96)	72 (51 to 88)
M10713 strain; N=24,17,16,12,23,15,35,24,25,158	39 (20 to 61)	40 (16 to 68)	49 (31 to 66)	46 (26 to 67)

End point values	B+R234_24_48	B48 50		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	175		
Units: Percentages of subjects				
number (confidence interval 95%)				
H44/76 strain; N=26,18,16,16,26,15,39,25,26,175	96 (80 to 100)	63 (55 to 70)		
5/99 strain; N=26,18,16,15,25,15,38,25,26,168	85 (65 to 96)	86 (80 to 91)		
NZ 98/254 strain; N=26,18,16,16,26,15,40,25,26,173	85 (65 to 96)	17 (12 to 24)		
M10713 strain; N=24,17,16,12,23,15,35,24,25,158	32 (15 to 54)	21 (15 to 28)		

Statistical analyses

No statistical analyses for this end point

Secondary: 11) Percentages of subjects with hSBA titers ≥1:5 and ≥1:8 after a third dose of rMenB+OMV NZ vaccine (at 4 years of age), in children who previously received 2 catch up doses of the same vaccine according to different schedules

End point title	11) Percentages of subjects with hSBA titers ≥1:5 and ≥1:8 after a third dose of rMenB+OMV NZ vaccine (at 4 years of age), in children who previously received 2 catch up doses of the same vaccine according to different schedules[16]

End point description:

The percentages of subjects with hSBA titers ≥1:5 and hSBA titers ≥1:8 at one month after a third dose of rMenB+OMV NZ vaccine was given to children, who had previously received 2 catch up doses (at 12,14 or 18,20 or 24,26 months) of the same vaccine according to different schedules, are reported.

Analysis was done on FAS (Immunogenicity).

End point type	Secondary

End point timeframe:

Day 31 (1 month post vaccination)

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: No statistical analysis is associated to this endpoint.

End point values	B12 14_48	B18 20_48	B24 26_48	B48 50
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	97	10	12	175
Units: Percentages of subjects				
number (confidence interval 95%)				
hSBA≥ 1:5 (H44/76 strain)	100 (96 to 100)	100 (69 to 100)	100 (74 to 100)	71 (64 to 78)
hSBA≥ 1:5 (5/99 strain; N=94,10,12,171)	100 (96 to 100)	100 (69 to 100)	100 (74 to 100)	90 (85 to 94)
hSBA≥ 1:5 (NZ 98/254 strain; N=95,10,12,173)	96 (90 to 99)	70 (35 to 93)	100 (74 to 100)	24 (18 to 31)
hSBA≥ 1:5 (M10713 strain; N=90,9,10,167)	93 (86 to 98)	100 (66 to 100)	90 (55 to 100)	77 (70 to 83)
hSBA≥ 1:8 (H44/76 strain)	100 (96 to 100)	100 (69 to 100)	100 (74 to 100)	63 (55 to 70)
hSBA≥ 1:8 (5/99 strain; N=94,10,12,171)	100 (96 to 100)	100 (69 to 100)	100 (74 to 100)	87 (81 to 92)
hSBA≥ 1:8 (NZ 98/254 strain; N=95,10,12,173)	95 (88 to 98)	60 (26 to 88)	100 (74 to 100)	17 (12 to 24)
hSBA≥ 1:8 (M10713 strain; N=90,9,10,167)	92 (85 to 97)	100 (66 to 100)	90 (55 to 100)	74 (67 to 81)

Statistical analyses

No statistical analyses for this end point

Secondary: 12) GMTs Following a Third Dose of rMenB+OMV NZ Vaccine in Children (at 4 Years of Age) Who Had Previously Received 2 Catch up Doses of the Same Vaccine According to Different Schedules

End point title	12) GMTs Following a Third Dose of rMenB+OMV NZ Vaccine in Children (at 4 Years of Age) Who Had Previously Received 2 Catch up Doses of the Same Vaccine According to Different Schedules[17]

End point description:

The GMTs, one month following a third dose of rMenB+OMV NZ vaccine in 4 year old children who had previously received 2 catch up doses (at 12,14 or 18,20 or 24,26 months) of the same vaccine according to different schedules, are reported.

Analysis was done on FAS (Immunogenicity).

End point type	Secondary

End point timeframe:

Day 31 (1 month post vaccination)

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: No statistical analysis is associated to this endpoint.

End point values	B12 14_48	B18 20_48	B24 26_48	B48 50
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	97	10	12	175
Units: Titers				
geometric mean (confidence interval 95%)				
H44/76 strain	154 (124 to 191)	145 (76 to 277)	211 (116 to 383)	11 (8.51 to 14)
5/99 strain; N= 94,10,12,171	1575 (1219 to 2034)	2381 (1112 to 5095)	3604 (1785 to 7278)	34 (27 to 42)
NZ 98/254 strain; N=95,10,12,173	31 (25 to 39)	18 (8.87 to 35)	47 (25 to 88)	2.25 (1.84 to 2.75)
M10713 strain; N=90,9,10,167	38 (29 to 49)	74 (34 to 164)	84 (39 to 180)	20 (15 to 25)

Statistical analyses

No statistical analyses for this end point

Secondary: 13) GMRs of GMTs in Children Following a Third Dose of rMenB+OMV NZ Vaccine (at 4 Years of Age) Who Previously Received 2 Catch up Doses of the Same Vaccine According to Different Schedules.

End point title	13) GMRs of GMTs in Children Following a Third Dose of rMenB+OMV NZ Vaccine (at 4 Years of Age) Who Previously Received 2 Catch up Doses of the Same Vaccine According to Different Schedules.[18]

End point description:

The GMRs of GMTs following a third dose of rMenB+OMV NZ vaccine (one month post 3rd dose/persistence at 48 months) in children who had previously received 2 catch up doses (at 12, 14 or 18, 20 or 24, 26 months) of the same vaccine according to different schedules are reported.

Analysis was done on FAS (Immunogenicity).

End point type	Secondary

End point timeframe:

Day 31 (1 month post 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: No statistical analysis is associated to this endpoint.

End point values	B12 14_48	B18 20_48	B24 26_48	B48 50
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	95	10	11	175
Units: Ratio				
geometric mean (confidence interval 95%)				
H44/76 strain	99 (79 to 125)	67 (34 to 135)	133 (68 to 258)	10 (8.2 to 13)
5/99 strain; N=92,10,11,168	70 (57 to 86)	51 (27 to 95)	55 (30 to 99)	29 (23 to 37)
NZ 98/254 strain; N=93,10,11,173	27 (21 to 36)	5.96 (2.7 to 13)	38 (18 to 81)	2.25 (1.84 to 2.75)
M10713 strain; N=88,9,9,158	5.24 (3.91 to 7.02)	7.06 (2.92 to 17)	7.35 (3.03 to 18)	2 (1.62 to 2.46)

Statistical analyses

No statistical analyses for this end point

Secondary: 14) Percentages of Subjects With a 4-fold Increase in hSBA Titers Following a Third Dose of rMenB+OMV NZ Vaccine Given at 4 Years of Age to Children Who Previously Received 2 Catch up Doses of the Same Vaccine

End point title	14) Percentages of Subjects With a 4-fold Increase in hSBA Titers Following a Third Dose of rMenB+OMV NZ Vaccine Given at 4 Years of Age to Children Who Previously Received 2 Catch up Doses of the Same Vaccine[19]

End point description:

The percentage of subjects with a four-fold increase in hSBA titers following a third dose of rMenB+OMV NZ vaccine, who had previously received 2 catch up doses (at 12, 14 or 18, 20 or 24, 26 months) of rMenB+OMV NZ vaccine according to different schedules,are reported.
Fourfold increase is defined as- for subjects with a pre-vaccination titer <1:2 to a post-vaccination titer ≥1:8 and for subjects with a pre-vaccination titer ≥1:2 to a post-vaccination titer ≥ 4 fold pre-vaccination titer.
Analysis was done on FAS (Immunogenicity).

End point type	Secondary

End point timeframe:

Day 31 (1 month post 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: No statistical analysis is associated to this endpoint.

End point values	B12 14_48	B18 20_48	B24 26_48	B48 50
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	95	10	11	175
Units: Percentages of subjects				
number (confidence interval 95%)				
H44/76 strain	99 (94 to 100)	90 (55 to 100)	100 (72 to 100)	63 (55 to 70)
5/99 strain; N=92,10,11,168	100 (96 to 100)	90 (55 to 100)	100 (72 to 100)	86 (80 to 91)
NZ 98/254 strain; N=93,10,11,173	94 (86 to 98)	50 (19 to 81)	100 (72 to 100)	17 (12 to 24)
M10713 strain; N=88,9,9,158	58 (47 to 68)	67 (30 to 93)	56 (21 to 86)	21 (15 to 28)

Statistical analyses

No statistical analyses for this end point

Secondary: 15) Percentages of Subjects With hSBA ≥1:5 and ≥1:8 in Response of Two Catch up Doses of rMenB+OMV NZ Vaccine When Administered to Children at 4 Years of Age

End point title	15) Percentages of Subjects With hSBA ≥1:5 and ≥1:8 in Response of Two Catch up Doses of rMenB+OMV NZ Vaccine When Administered to Children at 4 Years of Age[20]

End point description:

The sufficiency of immune response is reported in terms of percentages of subjects with hSBA ≥1:5 and ≥1:8 in response of two catch up doses of rMenB+OMV NZ vaccine, administered two months apart, in children at 4 years of age.
Immune response was considered sufficient if the lower limit of the two-sided 95% CI for the percentage of subjects achieving hSBA ≥ 1:5 at one month after the two-dose series was > 70% for all three indicator (H44/76; 5/99 and NZ 98/254) strains.
Immune sufficiency was not applicable for M10713 strain.
Analysis was done on FAS (Immunogenicity).

End point type	Secondary

End point timeframe:

Day 91 (1 month post second 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: No statistical analysis is associated to this endpoint.

End point values	B48 50			
Subject group type	Reporting group			
Number of subjects analysed	175			
Units: Percentages of subjects				
number (confidence interval 95%)				
hSBA≥ 1:5 (H44/76 strain)	100 (98 to 100)			
hSBA≥ 1:5 (5/99 strain)	100 (98 to 100)			
hSBA≥ 1:5 (NZ 98/254 strain; N=174)	91 (85 to 95)			
hSBA≥ 1:8 (H44/76 strain)	100 (98 to 100)			

hSBA≥ 1:8 (5/99 strain)	100 (98 to 100)			
hSBA≥ 1:8 (NZ 98/254 strain; N=174)	80 (73 to 86)			

Statistical analyses

No statistical analyses for this end point

Secondary: 16) GMTs Following 2 Catch up Doses of rMenB+OMV NZ Vaccine at 4 Years of Age

End point title	16) GMTs Following 2 Catch up Doses of rMenB+OMV NZ Vaccine at 4 Years of Age[21]

End point description:

The GMTs in children who received two catch up doses of rMenB+OMV NZ vaccine at 48 and 50 months of age are reported.
Analysis was done on FAS (Immunogenicity).

End point type	Secondary

End point timeframe:

Day 91 (1 month post second 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: No statistical analysis is associated to this endpoint.

End point values	B48 50			
Subject group type	Reporting group			
Number of subjects analysed	175			
Units: Titers				
geometric mean (confidence interval 95%)				
H44/76 strain	109 (98 to 120)			
5/99 strain	343 (302 to 389)			
NZ 98/254 strain; N=174	17 (14 to 19)			
M10713 strain; N=171	47 (40 to 56)			

Statistical analyses

No statistical analyses for this end point

Secondary: 17) GMRs of GMTs Following 2 Catch up Doses of rMenB+OMV NZ Vaccine at 4 Years of Age

End point title	17) GMRs of GMTs Following 2 Catch up Doses of rMenB+OMV NZ Vaccine at 4 Years of Age[22]

End point description:

The GMR of GMTs(one month post dose 2/baseline) in children following a two catch up dose of rMenB+OMV NZ at 48 and 50 months of age are reported.
Analysis was done on FAS (Immunogenicity).

End point type	Secondary

End point timeframe:

Day 91 (1 month post second vaccination)

Notes:

[22] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis is associated to this endpoint.

End point values	B48 50			
Subject group type	Reporting group			
Number of subjects analysed	175			
Units: Ratio				
geometric mean (confidence interval 95%)				
H44/76 strain	105 (94 to 116)			
5/99 strain; N=172	299 (256 to 350)			
NZ 98/254 strain; N=174	17 (14 to 19)			
M10713 strain; N=171	5.12 (3.95 to 6.65)			

Statistical analyses

No statistical analyses for this end point

Secondary: 18) Percentages of Subjects With 4-fold Increase in Serum Bactericidal Titers, Following 2 Catch up Doses of rMenB+OMV NZ Vaccine at 4 Years of Age

End point title	18) Percentages of Subjects With 4-fold Increase in Serum Bactericidal Titers, Following 2 Catch up Doses of rMenB+OMV NZ Vaccine at 4 Years of Age[23]

End point description:

The percentages of subjects with 4-fold increase in hSBA titers, one month following a two catch up dose of rMenB+OMV NZ at 4 years of age are reported.
Analysis was done on FAS (Immunogenicity).

End point type	Secondary

End point timeframe:

Day 91 (1 month post second vaccination)

Notes:

[23] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis is associated to this endpoint.

End point values	B48 50			
Subject group type	Reporting group			
Number of subjects analysed	175			
Units: Percentages of Subjects				
number (confidence interval 95%)				
H44/76 strain	100 (98 to 100)			
5/99 strain; N=172	99 (97 to 100)			

NZ 98/254 strain; N=174	80 (73 to 86)			
M10713 strain; N=161	51 (43 to 59)			

Statistical analyses

No statistical analyses for this end point

Secondary: 19) Number of Subjects Reporting Solicited Local and Systemic Adverse Events After Receiving a 5th Dose of rMenB+OMV NZ Vaccine (at 4 Years of Age)

End point title	19) Number of Subjects Reporting Solicited Local and Systemic Adverse Events After Receiving a 5th Dose of rMenB+OMV NZ Vaccine (at 4 Years of Age)[24]

End point description:

The safety and tolerability of the 5th dose rMenB+OMV NZ vaccine in children (at 4 years of age) who had previously received 3 primary doses (at 2, 3, 4, or 2, 4, 6 months) followed by a booster dose (at 12, 18 or 24 months) of rMenB+OMV NZ vaccine according to different schedules in the earlier studies is reported as number of subjects with solicited local and systemic adverse events.
Analysis was done on the safety population, ie, all subjects in the Exposed population who provided post vaccination and post-baseline safety data.

End point type	Secondary

End point timeframe:

From day 1 to day 7 after vaccination

Notes:

[24] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis is associated to this endpoint.

End point values	B+R246_12_48	B+R246_18_48	B+R246_24_48	B246_12_48
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	20	17	19
Units: Number of subjects				
Any local	27	18	17	16
Injection site Pain (mild)	4	5	1	6
Injection site Pain (moderate)	18	9	13	4
Injection site Pain (severe)	5	4	3	6
Injection site Erythema (25 - 50 mm)	2	3	3	5
Injection site Erythema (51 - 100 mm)	5	2	1	2
Injection site Erythema (>100 mm)	1	0	0	0
Injection site Induration (25 - 50 mm)	2	2	1	2
Injection site Induration (51 - 100 mm)	1	0	0	1
Injection site Induration (>100 mm)	1	0	0	0
Injection site Swelling (25 - 50 mm)	1	3	3	4
Injection site Swelling (51 - 100 mm)	1	0	1	2
Injection site Swelling (>100 mm)	1	0	0	0
Any Systemic	26	15	14	18
Change in eating habits	12	6	6	12
Rash	2	1	0	5
Arthralagia	12	4	6	9
Headache	5	1	6	3

Irritability	18	9	11	14
Diarrhea	4	1	1	2
Vomiting	0	1	0	0
Fever (≥ 38.0 °C)	6	3	3	2
Antipyretic used (prophylactically)	1	2	1	1
Antipyretic used (therapeutically)	5	5	4	3

End point values	B246_18_48	B246_24_48	B+R234_12_48	B+R234_18_48
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	27	17	43	29
Units: Number of subjects				
Any local	24	17	38	28
Injection site Pain (mild)	5	2	4	6
Injection site Pain (moderate)	14	9	24	14
Injection site Pain (severe)	4	5	10	8
Injection site Erythema (25 - 50 mm)	6	3	5	6
Injection site Erythema (51 - 100 mm)	7	3	10	6
Injection site Erythema (>100 mm)	1	1	2	0
Injection site Induration (25 - 50 mm)	5	2	6	7
Injection site Induration (51 - 100 mm)	2	1	2	1
Injection site Induration (>100 mm)	0	1	1	0
Injection site Swelling (25 - 50 mm)	5	3	7	7
Injection site Swelling (51 - 100 mm)	3	2	7	5
Injection site Swelling (>100 mm)	0	1	1	0
Any Systemic	19	13	36	27
Change in eating habits	7	8	20	11
Rash	2	4	7	5
Arthralagia	8	5	11	8
Headache	2	3	7	5
Irritability	13	8	23	20
Diarrhea	4	2	6	4
Vomiting	1	0	5	3
Fever (≥ 38.0 °C)	1	1	5	4
Antipyretic used (prophylactically)	2	1	7	1
Antipyretic used (therapeutically)	3	1	10	4

End point values	B+R234_24_48			
Subject group type	Reporting group			
Number of subjects analysed	27			
Units: Number of subjects				
Any local	27			
Injection site Pain (mild)	7			
Injection site Pain (moderate)	17			
Injection site Pain (severe)	3			
Injection site Erythema (25 - 50 mm)	5			

Injection site Erythema (51 - 100 mm)	3			
Injection site Erythema (>100 mm)	0			
Injection site Induration (25 - 50 mm)	6			
Injection site Induration (51 - 100 mm)	1			
Injection site Induration (>100 mm)	0			
Injection site Swelling (25 - 50 mm)	4			
Injection site Swelling (51 - 100 mm)	1			
Injection site Swelling (>100 mm)	0			
Any Systemic	23			
Change in eating habits	13			
Rash	2			
Arthralagia	12			
Headache	8			
Irritability	16			
Diarrhea	3			
Vomiting	2			
Fever (≥ 38.0 °C)	2			
Antipyretic used (prophylactically)	1			
Antipyretic used (therapeutically)	3			

Statistical analyses

No statistical analyses for this end point

Secondary: 20) Number of Subjects Reporting Solicited Local and Systemic Adverse Events After Receiving a 3rd Dose of rMenB+OMV NZ Vaccine (at 4 Years of Age)

End point title	20) Number of Subjects Reporting Solicited Local and Systemic Adverse Events After Receiving a 3rd Dose of rMenB+OMV NZ Vaccine (at 4 Years of Age)[25]

End point description:

The safety and tolerability of the 3rd dose rMenB+OMV NZ vaccine in children (at 4 years of age) who had previously received 2 catch up doses (at 12, 14 or 18, 20 or 24, 26 months) of rMenB+OMV NZ vaccine according to different schedules is reported as number of subjects with solicited local and systemic adverse events.
Analysis was done on the safety population.

End point type	Secondary

End point timeframe:

From day 1 to day 7 after vaccination

Notes:

[25] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis is associated to this endpoint.

End point values	B12 14_48	B18 20_48	B24 26_48	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	99	10	12	
Units: Number of Subjects				
Any local	94	9	11	
Injection site Pain (mild)	33	2	2	
Injection site Pain (moderate)	42	6	8	

Injection site Pain (severe)	19	1	1	
Injection site Erythema (25 - 50 mm)	12	2	0	
Injection site Erythema (51 - 100 mm)	7	1	0	
Injection site Erythema (>100 mm)	2	0	0	
Injection site Induration (25 - 50 mm)	8	1	0	
Injection site Induration (51 - 100 mm)	0	0	0	
Injection site Induration (>100 mm)	1	0	0	
Injection site Swelling (25 - 50 mm)	18	2	3	
Injection site Swelling (51 - 100 mm)	2	0	1	
Injection site Swelling (>100 mm)	0	0	0	
Any Systemic	78	6	9	
Change in eating habits	42	0	3	
Rash	13	0	0	
Arthralagia	28	1	6	
Headache	20	2	4	
Irritability	53	4	5	
Diarrhea	5	0	2	
Vomiting	6	2	1	
Fever (≥ 38.0 °C)	16	4	5	
Antipyretic used (prophylactically)	5	2	2	
Antipyretic used (therapeutically)	18	4	5	

Statistical analyses

No statistical analyses for this end point

Secondary: 21) Number of Subjects Reporting Solicited Local and Systemic Adverse Events After Receiving the first Catch up Dose of rMenB+OMV NZ Vaccine at 4 Years of Age

End point title	21) Number of Subjects Reporting Solicited Local and Systemic Adverse Events After Receiving the first Catch up Dose of rMenB+OMV NZ Vaccine at 4 Years of Age[26]

End point description:

The safety and tolerability of rMenB+OMV NZ vaccine in 4 year old children who received 2 catch up doses of rMenB+OMV NZ vaccine at 48 and 50 months, is reported as number of subjects with solicited local and systemic adverse events after the first dose.
Analysis was done on the safety population.

End point type	Secondary

End point timeframe:

From day 1 to day 7 after first vaccination

Notes:

[26] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis is associated to this endpoint.

End point values	B48 50			
Subject group type	Reporting group			
Number of subjects analysed	205			
Units: Number of Subjects				
Any local	186			
Injection site Pain (mild)	81			
Injection site Pain (moderate)	77			
Injection site Pain (severe)	27			
Injection site Erythema (25 - 50 mm)	34			
Injection site Erythema (51 - 100 mm)	8			
Injection site Erythema (>100 mm)	1			
Injection site Induration (25 - 50 mm)	23			
Injection site Induration (51-100 mm)	3			
Injection site Induration(>100 mm)	0			
Injection site Swelling (25 - 50 mm)	26			
Injection site Swelling (51 - 100 mm)	3			
Injection site Swelling (>100 mm)	1			
Any Systemic	137			
Rash	15			
Change in eating habits	49			
Headache	25			
Arthralagia	45			
Irritability	67			
Vomiting	8			
Diarrhea	11			
Fever (≥ 38.0 °C)	20			
Antipyretic used (prophylactically)	17			
Antipyretic used (therapeutically)	22			

Statistical analyses

No statistical analyses for this end point

Secondary: 22) Number of Subjects Reporting Solicited Local and Systemic Adverse Events After Receiving the second Catch up Dose of rMenB+OMV NZ Vaccine at 4 Years of Age

End point title	22) Number of Subjects Reporting Solicited Local and Systemic Adverse Events After Receiving the second Catch up Dose of rMenB+OMV NZ Vaccine at 4 Years of Age[27]

End point description:

The safety and tolerability of rMenB+OMV NZ vaccine in 4 year old children who received 2 catch up doses of rMenB+OMV NZ vaccine at 48 and 50 months, is reported as number of subjects with solicited local and systemic adverse events after the second dose.
Analysis was done on the safety population.

End point type	Secondary

End point timeframe:

From day 1 to day 7 after second vaccination

Notes:

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

Justification: No statistical analysis is associated to this endpoint.

End point values	B48 50			
Subject group type	Reporting group			
Number of subjects analysed	194			
Units: Number of Subjects				
Any local	161			
Injection site Pain (mild)	70			
Injection site Pain (moderate)	66			
Injection site Pain (severe)	21			
Injection site Erythema (25 - 50 mm)	15			
Injection site Erythema (51 - 100 mm)	19			
Injection site Erythema (>100 mm)	0			
Injection site Induration (25 - 50 mm)	16			
Injection site Induration (51-100 mm)	4			
Injection site Induration(>100 mm)	0			
Injection site Swelling (25 - 50 mm)	20			
Injection site Swelling (51 - 100 mm)	4			
Injection site Swelling (>100 mm)	0			
Any Systemic	108			
Rash	10			
Change in eating habits	43			
Headache	24			
Arthralagia	40			
Irritability	58			
Vomiting	6			
Diarrhea	8			
Fever (≥ 38.0 °C)	16			
Antipyretic used (prophylactically)	23			
Antipyretic used (therapeutically)	24			

Statistical analyses

No statistical analyses for this end point

Secondary: 23) Number of Subjects Reporting Unsolicited AEs After Receiving a 5th Dose of rMenB+OMV NZ Vaccine (at 4 Years of Age)

End point title	23) Number of Subjects Reporting Unsolicited AEs After Receiving a 5th Dose of rMenB+OMV NZ Vaccine (at 4 Years of Age)[28]

End point description:

The safety and tolerability of the 5th dose rMenB+OMV NZ vaccine in children (at 4 years of age) who had previously received 3 primary doses (at 2, 3, 4,or 2, 4, 6 months) followed by a booster dose (at 12, 18 or 24 months) of rMenB+OMV NZ vaccine according to different schedules in the earlier studies is reported as number of subjects with unsolicited AEs, Serious Adverse Events (SAE), AEs leading to premature withdrawal.
Analysis was done on the safety population.

End point type	Secondary

End point timeframe:

From day 1 to study termination

Notes:

[28] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis is associated to this endpoint.

End point values	B+R246_12_48	B+R246_18_48	B+R246_24_48	B246_12_48
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30	20	17	19
Units: Number of subjects				
Any AEs	8	4	4	7
SAEs	0	0	0	0
AEs leading to withdrawal	0	0	0	0

End point values	B246_18_48	B246_24_48	B+R234_12_48	B+R234_18_48
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	27	17	43	29
Units: Number of subjects				
Any AEs	7	3	11	11
SAEs	0	0	0	0
AEs leading to withdrawal	0	0	0	0

End point values	B+R234_24_48			
Subject group type	Reporting group			
Number of subjects analysed	28			
Units: Number of subjects				
Any AEs	6			
SAEs	0			
AEs leading to withdrawal	0			

Statistical analyses

No statistical analyses for this end point

Secondary: 24) Number of Subjects Reporting Unsolicited AEs After Receiving a 3rd Dose of rMenB+OMV NZ Vaccine (at 4 Years of Age)

End point title	24) Number of Subjects Reporting Unsolicited AEs After Receiving a 3rd Dose of rMenB+OMV NZ Vaccine (at 4 Years of Age)[29]

End point description:

The safety and tolerability of the 3rd dose rMenB+OMV NZ vaccine in children (at 4 years of age) who had previously received 2 catch up doses (at 12, 14 or 18, 20 or 24, 26 months) of rMenB+OMV NZ

vaccine according to different schedules is reported as number of subjects with Unsolicited AEs, Serious Adverse Events (SAEs), AEs leading to premature withdrawal.
Analysis was done on the safety population.

End point type	Secondary

End point timeframe:

From day 1 to study termination

Notes:

[29] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis is associated to this endpoint.

End point values	B12 14_48	B18 20_48	B24 26_48	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	100	11	12	
Units: Number of subjects				
Any AE	25	2	4	
SAEs	0	0	0	
AEs leading to withdrawal	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: 25) Number of Subjects Reporting Unsolicited AEs After Any Vaccination.

End point title	25) Number of Subjects Reporting Unsolicited AEs After Any Vaccination.[30]

End point description:

The safety and tolerability of the 3rd dose rMenB+OMV NZ vaccine in children (at 4 years of age) who had previously received 2 catch up doses (at 12, 14 or 18, 20 or 24, 26 months) of rMenB+OMV NZ vaccine according to different schedules is reported as number of subjects with unsolicited AEs, Serious Adverse Events (SAEs), AEs
leading to premature withdrawal.
Analysis was done on the safety population.

End point type	Secondary

End point timeframe:

From day 1 to study termination

Notes:

[30] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis is associated to this endpoint.

End point values	B48 50			
Subject group type	Reporting group			
Number of subjects analysed	206			
Units: Number of subjects				
Any AE	105			
SAEs	3			
AEs leading to premature withdrawal	1			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited (systematic) local and systemic adverse events (AEs), unsolicited (non-systematic) AEs and med. attended fever were recorded during the 7 days after study vaccination. Serious adverse events (SAEs) were collected throughout the study period.

Adverse event reporting additional description:

560 out of 805 enrolled subjects were exposed to study vaccination. Of these, 558 subjects were included in safety set.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	B+R246_18_48

Reporting group description:

Previously received rMenB+OMV NZ vaccine + routine vaccines at 2, 4 and 6 months of age followed by a booster dose of rMenB+OMV NZ vaccine at 18 months of age. One third of subjects from this group received a 5th dose of rMenB+OMV NZ vaccine in the present study at 4 years of age.

Reporting group title	B+R246_12_48

Reporting group description:

Previously received rMenB+OMV NZ vaccine + routine vaccines at 2, 4 and 6 months of age followed by a booster dose of rMenB+OMV NZ vaccine at 12 months of age. One third of subjects from this group received a 5th dose of rMenB+OMV NZ vaccine in the present study at 4 years of age.

Reporting group title	B+R246_24_48

Reporting group description:

Previously received rMenB+OMV NZ vaccine + routine vaccines at 2, 4 and 6 months of age followed by a booster dose of rMenB+OMV NZ vaccine at 24 months of age. One third of subjects from this group received a 5th dose of rMenB+OMV NZ vaccine in the present study at 4 years of age.

Reporting group title	B246_12_48

Reporting group description:

Previously received 3 doses of rMenB+OMV NZ vaccine at 2, 4 and 6 months of age and routine vaccines at 3, 5 and 7 months of age, followed by a booster dose of rMenB+OMV NZ vaccine at 12 months of age. One third of subjects from this group received a 5th dose of rMenB+OMV NZ vaccine in the present study at 4 years of age.

Reporting group title	B246_18_48

Reporting group description:

Previously received 3 doses of rMenB+OMV NZ vaccine at 2, 4 and 6 months of age and routine vaccines at 3, 5 and 7 months of age, followed by a booster dose of rMenB+OMV NZ vaccine at 18 months of age. One third of subjects from this group received a 5th dose of rMenB+OMV NZ vaccine in the present study at 4 years of age.

Reporting group title	B246_24_48

Reporting group description:

Previously received 3 doses of rMenB+OMV NZ vaccine at 2, 4 and 6 months of age and routine vaccines at 3, 5 and 7 months of age, followed by a booster dose of rMenB+OMV NZ vaccine at 24 months of age. One third of subjects from this group received a 5th dose of rMenB+OMV NZ vaccine in the present study at 4 years of age.

Reporting group title	B+R234_12_48

Reporting group description:

Previously received rMenB+OMV NZ vaccine + routine vaccines at 2, 3 and 4 months of age followed by a booster dose of rMenB+OMV NZ vaccine at 12months of age. All subjects received a 5th dose of rMenB+OMV NZ vaccine in the present study at 4 years of age.

Reporting group title	B+R234_18_48

Reporting group description:

Previously received rMenB+OMV NZ vaccine + routine vaccines at 2, 3 and 4 months of age followed by

a booster dose of rMenB+OMV NZ vaccine at 18 months of age. All subjects received a 5th dose of rMenB+OMV NZ vaccine in the present study at 4 years of age.

Reporting group title	B+R234_24_48

Reporting group description:

Previously received rMenB+OMV NZ vaccine + routine vaccines at 2, 3 and 4 months of age followed by a booster dose of rMenB+OMV NZ vaccine at 24 months of age. All subjects received a 5th dose of rMenB+OMV NZ vaccine in the present study at 4 years of age.

Reporting group title	B12 14_48

Reporting group description:

Previously received two catch-up doses of rMenB+OMV NZ vaccine at 12 &14 months of age. All subjects received a 3rd dose of rMenB+OMV NZ vaccine in the present study at 4 years of age.

Reporting group title	B18 20_48

Reporting group description:

Previously received two catch-up doses of rMenB+OMV NZ vaccine at 18 & 20 months of age. All subjects from this group received a 3rd dose of rMenB+OMV NZ vaccine in the present study at 4 years of age.

Reporting group title	B24 26_48

Reporting group description:

Previously received two catch-up doses of rMenB+OMV NZ vaccine at 24 & 26 months of age. All subjects from this group received a 3rd dose of rMenB+OMV NZ vaccine in the present study at 4 years of age.

Reporting group title	B48 50

Reporting group description:

Newly recruited 4 year old naive subjects who received 2 catch-up doses of rMenB+OMV NZ vaccine, two months apart, in the present study.

Serious adverse events	B+R246_18_48	B+R246_12_48	B+R246_24_48
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 20 (0.00%)	0 / 30 (0.00%)	0 / 17 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Concussion			
subjects affected / exposed	0 / 20 (0.00%)	0 / 30 (0.00%)	0 / 17 (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 / 20 (0.00%)	0 / 30 (0.00%)	0 / 17 (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
Periorbital haematoma			
subjects affected / exposed	0 / 20 (0.00%)	0 / 30 (0.00%)	0 / 17 (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			
Croup infectious			
subjects affected / exposed	0 / 20 (0.00%)	0 / 30 (0.00%)	0 / 17 (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	0 / 20 (0.00%)	0 / 30 (0.00%)	0 / 17 (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			
Dehydration			
subjects affected / exposed	0 / 20 (0.00%)	0 / 30 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	B246_12_48	B246_18_48	B246_24_48
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 19 (0.00%)	0 / 27 (0.00%)	0 / 17 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Concussion			
subjects affected / exposed	0 / 19 (0.00%)	0 / 27 (0.00%)	0 / 17 (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 / 19 (0.00%)	0 / 27 (0.00%)	0 / 17 (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
Periorbital haematoma			
subjects affected / exposed	0 / 19 (0.00%)	0 / 27 (0.00%)	0 / 17 (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			
Croup infectious			

subjects affected / exposed	0 / 19 (0.00%)	0 / 27 (0.00%)	0 / 17 (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	0 / 19 (0.00%)	0 / 27 (0.00%)	0 / 17 (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			
Dehydration			
subjects affected / exposed	0 / 19 (0.00%)	0 / 27 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	B+R234_12_48	B+R234_18_48	B+R234_24_48
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 43 (0.00%)	0 / 29 (0.00%)	0 / 28 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Concussion			
subjects affected / exposed	0 / 43 (0.00%)	0 / 29 (0.00%)	0 / 28 (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 / 43 (0.00%)	0 / 29 (0.00%)	0 / 28 (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
Periorbital haematoma			
subjects affected / exposed	0 / 43 (0.00%)	0 / 29 (0.00%)	0 / 28 (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			
Croup infectious			

subjects affected / exposed	0 / 43 (0.00%)	0 / 29 (0.00%)	0 / 28 (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	0 / 43 (0.00%)	0 / 29 (0.00%)	0 / 28 (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			
Dehydration			
subjects affected / exposed	0 / 43 (0.00%)	0 / 29 (0.00%)	0 / 28 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	B12 14_48	B18 20_48	B24 26_48
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 100 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Concussion			
subjects affected / exposed	0 / 100 (0.00%)	0 / 11 (0.00%)	0 / 12 (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 / 100 (0.00%)	0 / 11 (0.00%)	0 / 12 (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
Periorbital haematoma			
subjects affected / exposed	0 / 100 (0.00%)	0 / 11 (0.00%)	0 / 12 (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			
Croup infectious			

subjects affected / exposed	0 / 100 (0.00%)	0 / 11 (0.00%)	0 / 12 (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	0 / 100 (0.00%)	0 / 11 (0.00%)	0 / 12 (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			
Dehydration			
subjects affected / exposed	0 / 100 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	B48 50		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 206 (1.46%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Concussion			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Contusion			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Periorbital haematoma			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Croup infectious			

subjects affected / exposed	1 / 206 (0.49%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	B+R246_18_48	B+R246_12_48	B+R246_24_48
Total subjects affected by non-serious adverse events			
subjects affected / exposed	19 / 20 (95.00%)	29 / 30 (96.67%)	17 / 17 (100.00%)
Nervous system disorders			
Somnolence			
subjects affected / exposed	7 / 20 (35.00%)	18 / 30 (60.00%)	8 / 17 (47.06%)
occurrences (all)	7	18	8
Headache			
subjects affected / exposed	1 / 20 (5.00%)	5 / 30 (16.67%)	6 / 17 (35.29%)
occurrences (all)	1	5	6
General disorders and administration site conditions			
Injection site erythema			
alternative assessment type: Systematic			
subjects affected / exposed	13 / 20 (65.00%)	23 / 30 (76.67%)	13 / 17 (76.47%)
occurrences (all)	13	23	13
Injection site induration			
alternative assessment type: Systematic			
subjects affected / exposed	8 / 20 (40.00%)	21 / 30 (70.00%)	11 / 17 (64.71%)
occurrences (all)	8	24	11
Injection site pain			

alternative assessment type: Systematic			
subjects affected / exposed	19 / 20 (95.00%)	27 / 30 (90.00%)	17 / 17 (100.00%)
occurrences (all)	19	29	17
Injection site swelling			
alternative assessment type: Systematic			
subjects affected / exposed	7 / 20 (35.00%)	12 / 30 (40.00%)	10 / 17 (58.82%)
occurrences (all)	8	14	12
Pyrexia			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 20 (15.00%)	7 / 30 (23.33%)	3 / 17 (17.65%)
occurrences (all)	3	7	3
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 20 (0.00%)	0 / 30 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	1 / 20 (5.00%)	4 / 30 (13.33%)	1 / 17 (5.88%)
occurrences (all)	1	4	1
Vomiting			
subjects affected / exposed	1 / 20 (5.00%)	0 / 30 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 20 (0.00%)	0 / 30 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 20 (0.00%)	0 / 30 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Catarrh			
subjects affected / exposed	0 / 20 (0.00%)	0 / 30 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	0 / 20 (0.00%)	0 / 30 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Pruritus			

subjects affected / exposed	0 / 20 (0.00%)	0 / 30 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Rash			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 20 (5.00%)	2 / 30 (6.67%)	0 / 17 (0.00%)
occurrences (all)	1	2	0
Psychiatric disorders			
Eating disorders			
subjects affected / exposed	6 / 20 (30.00%)	12 / 30 (40.00%)	6 / 17 (35.29%)
occurrences (all)	7	12	6
Irritability			
subjects affected / exposed	9 / 20 (45.00%)	18 / 30 (60.00%)	11 / 17 (64.71%)
occurrences (all)	9	18	11
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	4 / 20 (20.00%)	12 / 30 (40.00%)	6 / 17 (35.29%)
occurrences (all)	4	12	6
Infections and infestations			
Acute tonsillitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 30 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Ear infection			
subjects affected / exposed	0 / 20 (0.00%)	0 / 30 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Erythema infectiosum			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 20 (0.00%)	0 / 30 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Gastroenteritis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 30 (3.33%)	0 / 17 (0.00%)
occurrences (all)	0	2	0
Influenza			
subjects affected / exposed	0 / 20 (0.00%)	0 / 30 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 20 (0.00%)	1 / 30 (3.33%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Viral infection			
subjects affected / exposed	0 / 20 (0.00%)	0 / 30 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	B246_12_48	B246_18_48	B246_24_48
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 19 (94.74%)	25 / 27 (92.59%)	17 / 17 (100.00%)
Nervous system disorders			
Somnolence			
subjects affected / exposed	9 / 19 (47.37%)	12 / 27 (44.44%)	6 / 17 (35.29%)
occurrences (all)	11	12	7
Headache			
subjects affected / exposed	3 / 19 (15.79%)	2 / 27 (7.41%)	3 / 17 (17.65%)
occurrences (all)	3	2	5
General disorders and administration site conditions			
Injection site erythema			
alternative assessment type: Systematic			
subjects affected / exposed	16 / 19 (84.21%)	21 / 27 (77.78%)	14 / 17 (82.35%)
occurrences (all)	17	23	15
Injection site induration			
alternative assessment type: Systematic			
subjects affected / exposed	14 / 19 (73.68%)	11 / 27 (40.74%)	12 / 17 (70.59%)
occurrences (all)	16	11	12
Injection site pain			
alternative assessment type: Systematic			
subjects affected / exposed	16 / 19 (84.21%)	23 / 27 (85.19%)	16 / 17 (94.12%)
occurrences (all)	16	26	16
Injection site swelling			
alternative assessment type: Systematic			
subjects affected / exposed	13 / 19 (68.42%)	10 / 27 (37.04%)	11 / 17 (64.71%)
occurrences (all)	13	10	11
Pyrexia			
alternative assessment type: Systematic			

subjects affected / exposed	2 / 19 (10.53%)	1 / 27 (3.70%)	1 / 17 (5.88%)
occurrences (all)	2	1	1
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 19 (5.26%)	0 / 27 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	1
Diarrhoea			
subjects affected / exposed	2 / 19 (10.53%)	4 / 27 (14.81%)	2 / 17 (11.76%)
occurrences (all)	2	4	2
Vomiting			
subjects affected / exposed	0 / 19 (0.00%)	1 / 27 (3.70%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 19 (10.53%)	0 / 27 (0.00%)	0 / 17 (0.00%)
occurrences (all)	2	0	0
Rhinorrhoea			
subjects affected / exposed	1 / 19 (5.26%)	0 / 27 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Catarrh			
subjects affected / exposed	0 / 19 (0.00%)	0 / 27 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	1 / 19 (5.26%)	0 / 27 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Pruritus			
subjects affected / exposed	1 / 19 (5.26%)	0 / 27 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Rash			
alternative assessment type: Systematic			
subjects affected / exposed	5 / 19 (26.32%)	2 / 27 (7.41%)	4 / 17 (23.53%)
occurrences (all)	6	2	4
Psychiatric disorders			
Eating disorders			

subjects affected / exposed	12 / 19 (63.16%)	7 / 27 (25.93%)	8 / 17 (47.06%)
occurrences (all)	12	7	9
Irritability			
subjects affected / exposed	14 / 19 (73.68%)	13 / 27 (48.15%)	8 / 17 (47.06%)
occurrences (all)	14	13	9
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	9 / 19 (47.37%)	8 / 27 (29.63%)	5 / 17 (29.41%)
occurrences (all)	10	8	5
Infections and infestations			
Acute tonsillitis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 27 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Ear infection			
subjects affected / exposed	0 / 19 (0.00%)	0 / 27 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Erythema infectiosum			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 19 (0.00%)	0 / 27 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 27 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 19 (0.00%)	0 / 27 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Nasopharyngitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 19 (0.00%)	0 / 27 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Viral infection			
subjects affected / exposed	0 / 19 (0.00%)	0 / 27 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	B+R234_12_48	B+R234_18_48	B+R234_24_48
Total subjects affected by non-serious			

adverse events			
subjects affected / exposed	42 / 43 (97.67%)	28 / 29 (96.55%)	27 / 28 (96.43%)
Nervous system disorders			
Somnolence			
subjects affected / exposed	22 / 43 (51.16%)	21 / 29 (72.41%)	14 / 28 (50.00%)
occurrences (all)	25	22	15
Headache			
subjects affected / exposed	7 / 43 (16.28%)	5 / 29 (17.24%)	8 / 28 (28.57%)
occurrences (all)	9	5	8
General disorders and administration site conditions			
Injection site erythema			
alternative assessment type: Systematic			
subjects affected / exposed	38 / 43 (88.37%)	24 / 29 (82.76%)	23 / 28 (82.14%)
occurrences (all)	40	24	23
Injection site induration			
alternative assessment type: Systematic			
subjects affected / exposed	24 / 43 (55.81%)	21 / 29 (72.41%)	19 / 28 (67.86%)
occurrences (all)	25	23	21
Injection site pain			
alternative assessment type: Systematic			
subjects affected / exposed	38 / 43 (88.37%)	28 / 29 (96.55%)	27 / 28 (96.43%)
occurrences (all)	40	30	30
Injection site swelling			
alternative assessment type: Systematic			
subjects affected / exposed	25 / 43 (58.14%)	17 / 29 (58.62%)	14 / 28 (50.00%)
occurrences (all)	25	18	15
Pyrexia			
alternative assessment type: Systematic			
subjects affected / exposed	7 / 43 (16.28%)	4 / 29 (13.79%)	2 / 28 (7.14%)
occurrences (all)	7	4	2
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 43 (0.00%)	0 / 29 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			

subjects affected / exposed	6 / 43 (13.95%)	4 / 29 (13.79%)	3 / 28 (10.71%)
occurrences (all)	6	4	3
Vomiting			
subjects affected / exposed	5 / 43 (11.63%)	3 / 29 (10.34%)	2 / 28 (7.14%)
occurrences (all)	7	3	2
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 43 (2.33%)	0 / 29 (0.00%)	0 / 28 (0.00%)
occurrences (all)	1	0	0
Rhinorrhoea			
subjects affected / exposed	1 / 43 (2.33%)	0 / 29 (0.00%)	0 / 28 (0.00%)
occurrences (all)	1	0	0
Catarrh			
subjects affected / exposed	0 / 43 (0.00%)	0 / 29 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	0 / 43 (0.00%)	0 / 29 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 43 (0.00%)	0 / 29 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Rash			
alternative assessment type: Systematic			
subjects affected / exposed	7 / 43 (16.28%)	5 / 29 (17.24%)	2 / 28 (7.14%)
occurrences (all)	7	5	2
Psychiatric disorders			
Eating disorders			
subjects affected / exposed	20 / 43 (46.51%)	11 / 29 (37.93%)	13 / 28 (46.43%)
occurrences (all)	23	12	14
Irritability			
subjects affected / exposed	23 / 43 (53.49%)	20 / 29 (68.97%)	16 / 28 (57.14%)
occurrences (all)	26	21	19
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	11 / 43 (25.58%)	8 / 29 (27.59%)	12 / 28 (42.86%)
occurrences (all)	11	8	12
Infections and infestations			
Acute tonsillitis			
subjects affected / exposed	0 / 43 (0.00%)	2 / 29 (6.90%)	0 / 28 (0.00%)
occurrences (all)	0	3	0
Ear infection			
subjects affected / exposed	0 / 43 (0.00%)	0 / 29 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1
Erythema infectiosum			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 43 (0.00%)	0 / 29 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 43 (0.00%)	0 / 29 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1
Influenza			
subjects affected / exposed	0 / 43 (0.00%)	0 / 29 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 43 (0.00%)	0 / 29 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Viral infection			
subjects affected / exposed	0 / 43 (0.00%)	0 / 29 (0.00%)	1 / 28 (3.57%)
occurrences (all)	0	0	1

Non-serious adverse events	B12 14_48	B18 20_48	B24 26_48
Total subjects affected by non-serious adverse events			
subjects affected / exposed	97 / 100 (97.00%)	10 / 11 (90.91%)	12 / 12 (100.00%)
Nervous system disorders			
Somnolence			
subjects affected / exposed	52 / 100 (52.00%)	3 / 11 (27.27%)	3 / 12 (25.00%)
occurrences (all)	56	3	3
Headache			

subjects affected / exposed	20 / 100 (20.00%)	2 / 11 (18.18%)	4 / 12 (33.33%)
occurrences (all)	22	2	4
General disorders and administration site conditions			
Injection site erythema			
alternative assessment type: Systematic			
subjects affected / exposed	73 / 100 (73.00%)	8 / 11 (72.73%)	7 / 12 (58.33%)
occurrences (all)	75	8	7
Injection site induration			
alternative assessment type: Systematic			
subjects affected / exposed	46 / 100 (46.00%)	6 / 11 (54.55%)	4 / 12 (33.33%)
occurrences (all)	48	7	4
Injection site pain			
alternative assessment type: Systematic			
subjects affected / exposed	94 / 100 (94.00%)	9 / 11 (81.82%)	11 / 12 (91.67%)
occurrences (all)	97	9	11
Injection site swelling			
alternative assessment type: Systematic			
subjects affected / exposed	46 / 100 (46.00%)	6 / 11 (54.55%)	7 / 12 (58.33%)
occurrences (all)	48	6	7
Pyrexia			
alternative assessment type: Systematic			
subjects affected / exposed	19 / 100 (19.00%)	5 / 11 (45.45%)	5 / 12 (41.67%)
occurrences (all)	19	5	7
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 100 (1.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Diarrhoea			
subjects affected / exposed	5 / 100 (5.00%)	0 / 11 (0.00%)	2 / 12 (16.67%)
occurrences (all)	5	0	2
Vomiting			
subjects affected / exposed	6 / 100 (6.00%)	2 / 11 (18.18%)	1 / 12 (8.33%)
occurrences (all)	6	2	1
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	1 / 100 (1.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 100 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Catarrh			
subjects affected / exposed	0 / 100 (0.00%)	1 / 11 (9.09%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	0 / 100 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 100 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Rash			
alternative assessment type: Systematic			
subjects affected / exposed	13 / 100 (13.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences (all)	15	0	0
Psychiatric disorders			
Eating disorders			
subjects affected / exposed	42 / 100 (42.00%)	0 / 11 (0.00%)	3 / 12 (25.00%)
occurrences (all)	43	0	3
Irritability			
subjects affected / exposed	53 / 100 (53.00%)	4 / 11 (36.36%)	5 / 12 (41.67%)
occurrences (all)	56	4	5
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	28 / 100 (28.00%)	1 / 11 (9.09%)	6 / 12 (50.00%)
occurrences (all)	28	1	6
Infections and infestations			
Acute tonsillitis			
subjects affected / exposed	0 / 100 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Ear infection			

subjects affected / exposed	3 / 100 (3.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences (all)	3	0	0
Erythema infectiosum			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 100 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 100 (0.00%)	1 / 11 (9.09%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Influenza			
subjects affected / exposed	0 / 100 (0.00%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 100 (0.00%)	0 / 11 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Viral infection			
subjects affected / exposed	1 / 100 (1.00%)	0 / 11 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1

Non-serious adverse events	B48 50		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	200 / 206 (97.09%)		
Nervous system disorders			
Somnolence			
subjects affected / exposed	105 / 206 (50.97%)		
occurrences (all)	150		
Headache			
subjects affected / exposed	40 / 206 (19.42%)		
occurrences (all)	58		
General disorders and administration site conditions			
Injection site erythema			
alternative assessment type: Systematic			
subjects affected / exposed	166 / 206 (80.58%)		
occurrences (all)	268		
Injection site induration			

alternative assessment type: Systematic			
subjects affected / exposed	117 / 206 (56.80%)		
occurrences (all)	185		
Injection site pain			
alternative assessment type: Systematic			
subjects affected / exposed	192 / 206 (93.20%)		
occurrences (all)	354		
Injection site swelling			
alternative assessment type: Systematic			
subjects affected / exposed	96 / 206 (46.60%)		
occurrences (all)	134		
Pyrexia			
alternative assessment type: Systematic			
subjects affected / exposed	36 / 206 (17.48%)		
occurrences (all)	45		
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
Diarrhoea			
subjects affected / exposed	18 / 206 (8.74%)		
occurrences (all)	21		
Vomiting			
subjects affected / exposed	15 / 206 (7.28%)		
occurrences (all)	16		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	11 / 206 (5.34%)		
occurrences (all)	12		
Rhinorrhoea			
subjects affected / exposed	0 / 206 (0.00%)		
occurrences (all)	0		
Catarrh			
subjects affected / exposed	0 / 206 (0.00%)		
occurrences (all)	0		

Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
Pruritus			
subjects affected / exposed	0 / 206 (0.00%)		
occurrences (all)	0		
Rash			
alternative assessment type: Systematic			
subjects affected / exposed	24 / 206 (11.65%)		
occurrences (all)	29		
Psychiatric disorders			
Eating disorders			
subjects affected / exposed	75 / 206 (36.41%)		
occurrences (all)	97		
Irritability			
subjects affected / exposed	91 / 206 (44.17%)		
occurrences (all)	135		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	67 / 206 (32.52%)		
occurrences (all)	86		
Infections and infestations			
Acute tonsillitis			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	2		
Ear infection			
subjects affected / exposed	6 / 206 (2.91%)		
occurrences (all)	7		
Erythema infectiosum			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
Gastroenteritis			
subjects affected / exposed	2 / 206 (0.97%)		
occurrences (all)	2		

Influenza			
subjects affected / exposed	1 / 206 (0.49%)		
occurrences (all)	1		
Nasopharyngitis			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 206 (1.46%)		
occurrences (all)	3		
Viral infection			
subjects affected / exposed	3 / 206 (1.46%)		
occurrences (all)	3		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 August 2012	1 - Modification of the inclusion criteria. 2 - Modification of the exclusion criteria to clarify the difference between exclusionary criteria and criteria that should be considered for delay of enrollment, vaccination, or blood sampling visits. 3 - Addition of missing abbreviations into the list. 4 - Editorial changes between: Exclusion Criteria, Vaccines Preparation and Administration, and Other Concomitant Treatment or Vaccines. Clarification of criteria for delay of subject enrollment, vaccination, and/or blood sampling visits under Exclusion Criteria. 5 - Addition and further clarification of missing collection time for immediate reactions post-vaccination for Group 7: Visit 1 and Visit 3. In addition, clarification of collections times for axillary body temperature, solicited local and systemic reactions. 6 - Correction of timing for reporting SAEs by investigator to the sponsor in compliance with EU directive. 7 - Standardizing visit window and clarification of visit window units as "days".
12 November 2012	1 - Modifying the 4th secondary objective upon introducing criteria for measuring sufficiency of immune response after two-dose series of rMenB+OMV NZ. 2 - Increasing the number of subjects planned for enrollment in group B_48 50 and adjusting total number of subjects planned accordingly. 3 - Introducing an interim analysis for group B_48 50. 4 - Editorial changes in one of the vaccine preparation and administration steps to be in alignment with instructions listed in the Investigator's Brochure (IB) and Summary of Product Characteristics (SmPC).
13 March 2013	1 - Add steps for collecting AEs related to study procedures (i.e. Blood draw) for subjects belonging to the non-vaccination subset#1 of groups 1 and 2, who are assigned to have a single blood draw visit. 2 - Clarify study visit windows.
14 November 2013	Definition of the End of Study in relation to the testing of the last biological sample collected from the study subjects.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported