

**Clinical trial results:**

Title of the trial: A Phase 3, Open-Label, Multi-Center, Extension Study of V72P13E1 to Assess Antibody Persistence at One Year After a Fourth Dose Boost or Two Catch-Up Doses of Novartis Meningococcal B Recombinant Vaccine Administered Starting at 12 Months of Age and to Evaluate the Response to a Third Dose Boost or Two Catch-Up Doses Starting at 24 Months of Age.

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

Summary

EudraCT number	2009-018101-52
Trial protocol	FI CZ
Global end of trial date	08 September 2011

Results information

Result version number	v2 (current)
This version publication date	01 June 2016
First version publication date	26 December 2014
Version creation reason	

Trial information**Trial identification**

Sponsor protocol code	V72P13E2
-----------------------	----------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01139021
WHO universal trial number (UTN)	-

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMA-000139-PIP01-07
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No	Yes

1901/2006 apply to this trial?

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	02 May 2012
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	08 September 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Immunogenicity: To explore antibody persistence at one year after a booster (fourth) dose of rMenB+OMV NZ, administered at 12 months of age to toddlers enrolled in study V72P13E1 who previously received a three-dose primary series of rMenB+OMV NZ (administered at 2, 4, and 6 months of age) as infants in the original parent study V72P13.

Protection of trial subjects:

This clinical study was designed, implemented and reported in accordance with the ICH Harmonized Tripartite Guidelines for GCP, with applicable local regulations, including the European Directive 2001/20/EC, the US CFR Title 21, and the Japanese Ministry of Health, Labor, and Welfare, Novartis codes on the protection of human rights, and with the ethical principles laid down in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 June 2010
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	6 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Czech Republic: 345
Country: Number of subjects enrolled	Finland: 163
Worldwide total number of subjects	508
EEA total number of subjects	508

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0

Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	42
Children (2-11 years)	466
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:

Participants were enrolled from two study centers.

Pre-assignment

Screening details:

The eligible subjects from V72P13E1 (NCT00847145) who originally participated in the open-label, immunogenicity subset of parent study V72P13 (NCT00657709) and a naïve group, at 24 months of age, who did not previously participate in V72P13 (or V72P13E1) were enrolled in this study.

Period 1

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

Blinding implementation details:

Not Applicable

Arms

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

Arm title	B246_12M12
------------------	------------

Arm description:

Subjects assessed one year post administration of rMenB+OMV NZ and Measles, Mumps, Rubella, Varicella (MMRV) at 12th month after primary vaccination at 2nd ,4th and 6th months of age.

Arm type	Experimental
Investigational medicinal product name	Not Applicable
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Each dose 0.5 mL of injectable solution was administered intramuscularly.

Arm title	B246_12M13
------------------	------------

Arm description:

Subjects assessed one year post administration of rMenB+OMV NZ at 12th month and MMRV at 13th month after primary vaccination at 2nd ,4th and 6th months of age.

Arm type	Experimental
Investigational medicinal product name	Not Applicable
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Each dose 0.5 mL of injectable solution was administered intramuscularly.

Arm title	B13_15_27
------------------	-----------

Arm description:

Subjects assessed at 12 months after two catch-up doses of rMenB+OMV NZ administered to children at 13th and 15th months of age and MMRV at 12th month; at 1 month and 6 months post booster dose administered at 27 months of age.

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

Investigational medicinal product name	rMenB+OMV NZ
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
Each dose 0.5 mL of injectable solution was administered intramuscularly.	
Arm title	B12_14_26

Arm description:

Subjects assessed at 12 months after two catch-up doses of rMenB+OMV NZ administered to children at either 12th and 14th months of age and MMRV at 12th month; at 1 month and 6 months post booster dose administered at 26 months of age.

Arm type	Experimental
Investigational medicinal product name	rMenB+OMV NZ
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
Each dose 0.5 mL of injectable solution was administered intramuscularly.	
Arm title	B_24_26

Arm description:

Subjects assessed at 1 month and 6 months post two catch-up doses of rMenB+OMV NZ administered to naive children at 24 and 26 months of age

Arm type	Experimental
Investigational medicinal product name	rMenB+OMV NZ
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
Each dose 0.5 mL of injectable solution was administered intramuscularly.	
Arm title	B12M13

Arm description:

Subject was randomized in group B13_15_27 but treated as group B12_M13

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

Dosage and administration details:

Each dose 0.5 mL of injectable solution was administered intramuscularly.

Number of subjects in period 1	B246_12M12	B246_12M13	B13_15_27
Started	152	153	67
Completed	151	153	67
Not completed	1	0	0
Consent withdrawn by subject	-	-	-
Adverse Event	-	-	-
Lost to follow-up	-	-	-
Protocol deviation	1	-	-

Number of subjects in period 1	B12_14_26	B_24_26	B12M13
Started	19	116	1
Completed	18	107	1
Not completed	1	9	0
Consent withdrawn by subject	1	4	-
Adverse Event	-	1	-
Lost to follow-up	-	2	-
Protocol deviation	-	2	-

Baseline characteristics

Reporting groups

Reporting group title	B246_12M12
Reporting group description:	
Subjects assessed one year post administration of rMenB+OMV NZ and Measles, Mumps, Rubella, Varicella (MMRV) at 12th month after primary vaccination at 2nd ,4th and 6th months of age.	
Reporting group title	B246_12M13
Reporting group description:	
Subjects assessed one year post administration of rMenB+OMV NZ at 12th month and MMRV at 13th month after primary vaccination at 2nd ,4th and 6th months of age.	
Reporting group title	B13_15_27
Reporting group description:	
Subjects assessed at 12 months after two catch-up doses of rMenB+OMV NZ administered to children at 13th and 15th months of age and MMRV at 12th month; at 1 month and 6 months post booster dose administered at 27 months of age.	
Reporting group title	B12_14_26
Reporting group description:	
Subjects assessed at 12 months after two catch-up doses of rMenB+OMV NZ administered to children at either 12th and 14th months of age and MMRV at 12th month; at 1 month and 6 months post booster dose administered at 26 months of age.	
Reporting group title	B_24_26
Reporting group description:	
Subjects assessed at 1 month and 6 months post two catch-up doses of rMenB+OMV NZ administered to naive children at 24 and 26 months of age	
Reporting group title	B12M13
Reporting group description:	
Subject was randomized in group B13_15_27 but treated as group B12_M13	

Reporting group values	B246_12M12	B246_12M13	B13_15_27
Number of subjects	152	153	67
Age categorical Units: Subjects			

Age continuous Units: months			
arithmetic mean	25	25.3	27.3
standard deviation	± 1	± 0.9	± 0.9
Gender categorical Units: Subjects			
Female	65	85	30
Male	87	68	37

Reporting group values	B12_14_26	B_24_26	B12M13
Number of subjects	19	116	1
Age categorical Units: Subjects			

Age continuous Units: months arithmetic mean standard deviation	26.6 ± 1.2	24.7 ± 1.4	26 ± 0
Gender categorical Units: Subjects			
Female	10	55	1
Male	9	61	0

Reporting group values	Total		
Number of subjects	508		
Age categorical Units: Subjects			

Age continuous Units: months arithmetic mean standard deviation	-		
Gender categorical Units: Subjects			
Female	246		
Male	262		

End points

End points reporting groups

Reporting group title	B246_12M12
Reporting group description: Subjects assessed one year post administration of rMenB+OMV NZ and Measles, Mumps, Rubella, Varicella (MMRV) at 12th month after primary vaccination at 2nd ,4th and 6th months of age.	
Reporting group title	B246_12M13
Reporting group description: Subjects assessed one year post administration of rMenB+OMV NZ at 12th month and MMRV at 13th month after primary vaccination at 2nd ,4th and 6th months of age.	
Reporting group title	B13_15_27
Reporting group description: Subjects assessed at 12 months after two catch-up doses of rMenB+OMV NZ administered to children at 13th and 15th months of age and MMRV at 12th month; at 1 month and 6 months post booster dose administered at 27 months of age.	
Reporting group title	B12_14_26
Reporting group description: Subjects assessed at 12 months after two catch-up doses of rMenB+OMV NZ administered to children at either 12th and 14th months of age and MMRV at 12th month; at 1 month and 6 months post booster dose administered at 26 months of age.	
Reporting group title	B_24_26
Reporting group description: Subjects assessed at 1 month and 6 months post two catch-up doses of rMenB+OMV NZ administered to naive children at 24 and 26 months of age	
Reporting group title	B12M13
Reporting group description: Subject was randomized in group B13_15_27 but treated as group B12_M13	
Subject analysis set title	Enrolled Population
Subject analysis set type	Modified intention-to-treat
Subject analysis set description: All subjects who were enrolled in this study.	
Subject analysis set title	Safety Population Included
Subject analysis set type	Safety analysis
Subject analysis set description: All subjects enrolled who had received at least one rMenB+OMV NZ vaccination and provided post-baseline safety data.	
Subject analysis set title	Modified ITT (Primary)
Subject analysis set type	Modified intention-to-treat
Subject analysis set description: All subjects in the enrolled population who provided an evaluable serum sample (visit 1, i.e., 12 months after booster or 2 dose catch-up schedule or prior to vaccination naive controls). In case of randomization errors, subjects were to be analyzed as planned in MITT population	
Subject analysis set title	Modified ITT (Secondary)
Subject analysis set type	Modified intention-to-treat
Subject analysis set description: All subjects in the enrolled population who: actually received a study vaccination, and provided at least an evaluable serum sample after vaccination (groups B13_15_27 and B12_14_26, visit 2), or at least an evaluable serum sample before vaccination and 30 days after the second vaccination (B24_26). In case of randomization errors, subjects were to be analyzed as planned in MITT population	
Subject analysis set title	B246_12Tot
Subject analysis set type	Modified intention-to-treat
Subject analysis set description: Subjects assessed one year post administration of rMenB+OMV NZ at 12th month and MMRV at 12th or 13th month after primary vaccination at 2nd ,4th and 6th months of age	

Subject analysis set title	B12+B13Tot
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

Subjects assessed at 12 months after two catch-up doses of rMenB+OMV NZ administered to children at either 12th and 14th or 13th and 15th months of age and MMRV at 12th month; at 1 month and 6 months post booster dose administered at 26th or 27th months of age.

Primary: Geometric Mean Titers (GMTs) to assess antibody persistence at one year after a booster dose of rMenB+OMV NZ Vaccination

End point title	Geometric Mean Titers (GMTs) to assess antibody persistence at one year after a booster dose of rMenB+OMV NZ Vaccination ^{[1][2]}
-----------------	--

End point description:

To assess the immunogenicity in terms of human Serum Bactericidal Assay (hSBA) GMTs, through antibody persistence at one year after a booster (fourth) dose of rMenB+OMV NZ in groups that received a three-dose primary series at 2, 4,6 months of age. Group B246_12M12 received MMRV at 12 months of age (concomitantly) and group B246_12M13 received MMRV at 13 months of age (separately). Analysis was done on Modified Intention-To-Treat (MITT) population (Primary).

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

End point timeframe:

12 months post booster (4th) vaccination.

Notes:

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

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

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

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

End point values	B246_12M12	B246_12M13	B246_12Tot	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	147	153	300	
Units: Titers				
geometric mean (confidence interval 95%)				
H44/76-SL (N=147,152,299)	7.38 (5.55 to 9.83)	8.3 (6.17 to 11)	6.5 (5.63 to 7.5)	
5/99 (N=147,151,298)	68 (52 to 91)	90 (67 to 121)	81 (71 to 94)	
NZ98/254 (N=147,153,300)	1.57 (1.24 to 1.99)	1.79 (1.4 to 2.29)	1.91 (1.7 to 2.15)	
M10713 (N=143,148,291)	4.37 (3.24 to 5.9)	3.62 (2.65 to 4.94)	3.35 (2.88 to 3.9)	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of subjects with hSBA $\geq 1:5$ and hSBA $\geq 1:8$ to assess antibody persistence at one year after a booster dose of rMenB+OMV NZ Vaccination

End point title	Percentage of subjects with hSBA $\geq 1:5$ and hSBA $\geq 1:8$ to assess antibody persistence at one year after a booster dose of rMenB+OMV NZ Vaccination ^{[3][4]}
-----------------	---

End point description:

To assess the immunogenicity in terms of percentage of subjects with hSBA $\geq 1:5$ & hSBA $\geq 1:8$ through

antibody persistence at 1 year after a booster (4th) dose of rMenB+OMV NZ in groups that received a three-dose primary series at 2,4,6 months of age. Group B246_12M12 received MMRV at 12 months (concomitantly) & B246_12M13 received MMRV at 13 months of age (separately).

Analysis was done on MITT population (Primary).

End point type	Primary
End point timeframe:	
12 months post booster (4th) vaccination.	

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

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

End point values	B246_12M12	B246_12M13	B246_12Tot	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	147	153	300	
Units: Percentage of subjects				
number (confidence interval 95%)				
H44/76-SL (hSBA $\geq 1:5$) (N=147, 152, 299)	60 (51 to 68)	64 (56 to 71)	62 (56 to 67)	
5/99 (hSBA $\geq 1:5$) (N=147, 151, 298)	96 (91 to 98)	99 (95 to 100)	97 (95 to 99)	
NZ98/254 (hSBA $\geq 1:5$) (N=147, 153, 300)	18 (12 to 25)	17 (11 to 24)	17 (13 to 22)	
M10713 (hSBA $\geq 1:5$) (N=143, 148, 291)	40 (32 to 48)	32 (25 to 41)	36 (31 to 42)	
H44/76-SL (hSBA $\geq 1:8$) (N=147, 152, 299)	44 (35 to 52)	47 (39 to 55)	45 (39 to 51)	
5/99 (hSBA $\geq 1:8$) (N=147, 151, 298)	96 (91 to 98)	98 (94 to 100)	97 (94 to 99)	
NZ98/254 (hSBA $\geq 1:8$) (N=147, 153, 300)	12 (7 to 19)	14 (9 to 21)	13 (10 to 18)	
M10713 (hSBA $\geq 1:8$) (N=143, 148, 291)	31 (23 to 39)	24 (17 to 31)	27 (22 to 33)	

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean concentrations (GMCs) to assess antibody persistence at one year after a booster dose of rMenB+OMV NZ Vaccination

End point title	Geometric Mean concentrations (GMCs) to assess antibody persistence at one year after a booster dose of rMenB+OMV NZ Vaccination ^{[5][6]}
-----------------	--

End point description:

To assess the immunogenicity in terms of GMCs determined by ELISA through antibody persistence at one year after a booster (fourth) dose of rMenB+OMV NZ in groups that received a three-dose primary series at 2, 4,6 months of age. Group B246_12M12 received MMRV at 12 months of age (concomitantly) and group B246_12M13 received MMRV at 13 months of age (separately) against vaccine antigen 287-953.

Analysis was done on MITT population (Primary).

End point type	Primary
End point timeframe:	
12 months post booster (4th) vaccination	

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

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

End point values	B246_12M12	B246_12M13	B246_12Tot	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	148	153	301	
Units: Concentration				
geometric mean (confidence interval 95%)				
287-953	360 (293 to 442)	389 (314 to 482)	352 (317 to 391)	

Statistical analyses

No statistical analyses for this end point

Secondary: GMTs to assess antibody persistence at 12 months after two catch-up doses and 6 months after booster dose of rMenB+OMV NZ Vaccination

End point title	GMTs to assess antibody persistence at 12 months after two catch-up doses and 6 months after booster dose of rMenB+OMV NZ Vaccination ^[7]
-----------------	--

End point description:

To assess the immunogenicity in terms of hSBA GMTs at 12 months after two catch up doses previously administered to children at either 12 and 14 or 13 and 15 months of age and 6 months after a booster dose of rMenB+OMV NZ administered at 26 or 27 months of age. Both the groups received MMRV at 12 months of age.

Analysis was done on MITT population (Secondary).

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

End point timeframe:

6 months or 12 months post two catch-up dose vaccination.

Notes:

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

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

End point values	B13_15_27	B12_14_26	B12+B13Tot	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	67	18	85	
Units: Titers				
geometric mean (confidence interval 95%)				
H44/76-SL (12months) (N= 67, 18, 85)	14 (9.01 to 23)	8.4 (4.13 to 17)	10 (8 to 13)	
5/99 (12months) (N= 67, 18, 85)	73 (43 to 123)	71 (32 to 154)	65 (49 to 85)	
NZ98/254 (12months) (N= 67, 18, 85)	1.67 (1.09 to 2.55)	1.2 (0.64 to 2.27)	1.75 (1.39 to 2.2)	
M10713 (12months) (N= 64, 18, 82)	3.74 (2.14 to 6.54)	3.29 (1.43 to 7.56)	3.4 (2.5 to 4.61)	
H44/76-SL (6months) (N= 67, 17, 84)	68 (41 to 113)	70 (32 to 151)	51 (38 to 68)	

5/99 (6months) (N= 67, 17, 84)	524 (332 to 827)	525 (263 to 1047)	518 (405 to 664)	
NZ98/254 (6months) (N= 67, 17, 84)	8.87 (5.23 to 15)	16 (7.13 to 35)	8.8 (6.63 to 12)	
M10713 (6months) (N= 66, 16, 82)	30 (18 to 49)	36 (17 to 78)	26 (20 to 33)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with hSBA $\geq 1:5$ and hSBA $\geq 1:8$ to assess antibody persistence at 12 months after two catch up doses and 6 months after a booster doses of rMenB+OMV NZ Vaccination.

End point title	Percentage of subjects with hSBA $\geq 1:5$ and hSBA $\geq 1:8$ to assess antibody persistence at 12 months after two catch up doses and 6 months after a booster doses of rMenB+OMV NZ Vaccination. ^[8]
-----------------	---

End point description:

To assess the immunogenicity in terms of percentage of subjects with hSBA $\geq 1:5$ and hSBA $\geq 1:8$ at 12 months after two catch up doses previously administered to children at either 12 and 14 or 13 and 15 months of age and 6 months after a booster dose of rMenB+OMV NZ administered at 26 or 27 months of age. Both the groups received MMRV at 12 months of age.

Analysis was done on MITT population (Secondary).

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

End point timeframe:

6month and 12 months post two catch-up dose vaccination.

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: There was no statistical null hypothesis associated with this immunogenicity objective.

End point values	B13_15_27	B12_14_26	B12+B13Tot	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	67	18	85	
Units: Percentage of subjects				
number (confidence interval 95%)				
H44/76-SL (hSBA $\geq 1:5$) (12months) (N= 67, 18, 85)	75 (63 to 84)	56 (31 to 78)	71 (60 to 80)	
5/99 (hSBA $\geq 1:5$) (12months) (N= 67, 18, 85)	97 (90 to 100)	94 (73 to 100)	96 (90 to 99)	
NZ98/254 (hSBA $\geq 1:5$) (12months) (N= 67, 18, 85)	18 (10 to 29)	6 (0 to 27)	15 (8 to 25)	
M10713 (hSBA $\geq 1:5$) (12months) (N= 64, 18, 82)	39 (27 to 52)	28 (10 to 53)	37 (26 to 48)	
H44/76-SL (hSBA $\geq 1:5$) (6months) (N= 67, 17, 84)	99 (92 to 100)	100 (80 to 100)	99 (94 to 100)	
5/99 (hSBA $\geq 1:5$) (6months) (N= 67, 18, 84)	100 (95 to 100)	100 (80 to 100)	100 (96 to 100)	
NZ98/254 (hSBA $\geq 1:5$) (6months) (N= 67, 18, 84)	73 (61 to 83)	82 (57 to 96)	75 (64 to 84)	
M10713 (hSBA $\geq 1:5$) (6months) (N= 66, 16, 82)	92 (83 to 97)	94 (70 to 100)	93 (85 to 97)	
H44/76-SL (hSBA $\geq 1:8$) (12months) (N= 67, 18, 85)	63 (50 to 74)	56 (31 to 78)	61 (50 to 72)	

5/99 (hSBA $\geq 1:8$) (12months) (N= 67, 18, 85)	96 (87 to 99)	94 (73 to 100)	95 (88 to 99)	
NZ98/254 (hSBA $\geq 1:8$) (12months) (N= 67, 18, 85)	15 (7 to 26)	6 (0 to 27)	13 (7 to 22)	
M10713 (hSBA $\geq 1:8$) (12months) (N= 64, 18, 82)	27 (16 to 39)	22 (6 to 48)	26 (17 to 36)	
H44/76-SL (hSBA $\geq 1:8$) (6months) (N= 67, 17, 84)	91 (82 to 97)	100 (80 to 100)	93 (85 to 97)	
5/99 (hSBA $\geq 1:8$) (6months) (N= 67, 18, 84)	100 (95 to 100)	94 (71 to 100)	99 (94 to 100)	
NZ98/254 (hSBA $\geq 1:8$) (6months) (N= 67, 18, 84)	52 (40 to 65)	65 (38 to 86)	55 (44 to 66)	
M10713 (hSBA $\geq 1:8$) (6months) (N= 66, 16, 82)	86 (76 to 94)	81 (54 to 96)	85 (76 to 92)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with at least four fold increase in hSBA titers to evaluate antibody response 1 month post booster dose of rMenB+OMV NZ Vaccination

End point title	Percentage of subjects with at least four fold increase in hSBA titers to evaluate antibody response 1 month post booster dose of rMenB+OMV NZ Vaccination ^[9]
-----------------	---

End point description:

To assess the immunogenicity in terms of percentage of subjects with at least four fold increase in hSBA titers 1 month post booster dose of rMenB+OMV NZ administered at 26 or 27 months of age, in children previously administered two catch-up doses of rMenB+OMV NZ at either 12 and 14 or 13 and 15 months of age. Both the groups received MMRV at 12 months of age.

Analysis was done on MITT population (Secondary).

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

End point timeframe:

1 month post booster dose versus prebooster

Notes:

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

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

End point values	B13_15_27	B12_14_26	B12+B13Tot	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	67	18	85	
Units: Percentage of Subjects				
number (confidence interval 95%)				
H44/76-SL (N= 66, 18, 84)	100 (95 to 100)	100 (81 to 100)	100 (96 to 100)	
5/99 (N= 67, 18, 85)	99 (92 to 100)	100 (81 to 100)	99 (94 to 100)	
NZ98/254 (N= 65, 18, 83)	97 (89 to 100)	94 (73 to 100)	96 (90 to 99)	
M10713 (N= 62, 16, 78)	82 (70 to 91)	88 (62 to 98)	83 (73 to 91)	

Statistical analyses

No statistical analyses for this end point

Secondary: GMCs to assess antibody persistence at one year after two catch-up doses and 6 months after booster of rMenB+OMV NZ Vaccination against 287-953 strain.

End point title	GMCs to assess antibody persistence at one year after two catch-up doses and 6 months after booster of rMenB+OMV NZ Vaccination against 287-953 strain. ^[10]
-----------------	---

End point description:

To assess the immunogenicity in terms of GMCs determined by ELISA at 12 months after two catch up doses previously administered to children at either 12 and 14 or 13 and 15 months of age and 6 months after a booster dose of rMenB+OMV NZ administered at 26 or 27 months of age. Both the groups received MMRV at 12 months of age.

Analysis was done on MITT population (Secondary).

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

End point timeframe:

12 months post two catch-up dose vaccination and 6 months post booster dose

Notes:

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

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

End point values	B13_15_27	B12_14_26	B12+B13Tot	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	67	18	85	
Units: Concentration				
geometric mean (confidence interval 95%)				
287-953 (12months) (N=67, 18, 85)	219 (149 to 322)	246 (138 to 437)	227 (185 to 278)	
287-953 (6months) (N=67, 17, 84)	2314 (1596 to 3355)	3259 (1859 to 5712)	2597 (2104 to 3205)	

Statistical analyses

No statistical analyses for this end point

Secondary: GMTs to characterize antibody response at 1 month and 6 months post two catch-up doses of rMenB+OMV NZ administered to naive children at 24 and 26 months of age.

End point title	GMTs to characterize antibody response at 1 month and 6 months post two catch-up doses of rMenB+OMV NZ administered to naive children at 24 and 26 months of age. ^[11]
-----------------	---

End point description:

To assess the immunogenicity in terms of GMTs through antibody response at 1 month and 6 months post two catch-up doses of rMenB+OMV NZ administered to naive children at 24 and 26 months of age. Analysis was done on MITT population (Secondary).

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

End point timeframe:

1 month and 6 months post two catch-up doses.

Notes:

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

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

End point values	B_24_26			
Subject group type	Reporting group			
Number of subjects analysed	108			
Units: Titers				
geometric mean (confidence interval 95%)				
H44/76-SL (1 month) (N= 105)	220 (186 to 261)			
5/99 (1 month) (N= 103)	455 (372 to 556)			
NZ98/254 (1 month) (N=108)	27 (23 to 32)			
M10713 (1 month) (N=100)	38 (32 to 45)			
H44/76-SL (6 months) (N=104)	22 (18 to 27)			
5/99 (6 months) (N= 104)	71 (57 to 89)			
NZ98/254 (6 months) (N= 104)	1.88 (1.57 to 2.26)			
M10713 (6 months) (N= 104)	8.04 (6.39 to 10)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with hSBA $\geq 1:5$ and hSBA $\geq 1:8$ to assess antibody response at 1 month and 6 month post two catch-up doses of rMenB+OMV NZ administered to naive children at 24 and 26 months of age

End point title	Percentage of subjects with hSBA $\geq 1:5$ and hSBA $\geq 1:8$ to assess antibody response at 1 month and 6 month post two catch-up doses of rMenB+OMV NZ administered to naive children at 24 and 26 months of age ^[12]
-----------------	--

End point description:

To assess the immunogenicity in terms of percentage of subjects with hSBA $\geq 1:5$ and hSBA $\geq 1:8$ through antibody response at at 1 month and 6 month post two catch-up doses of rMenB+OMV NZ administered to naive children at 24 and 26 months of age.

Analysis was done on MITT population (Secondary).

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

End point timeframe:

1 month and 6 months post two catch-up doses

Notes:

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

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

End point values	B_24_26			
Subject group type	Reporting group			
Number of subjects analysed	108			
Units: Percentage of subjects				
number (confidence interval 95%)				
H44/76-SL (hSBA $\geq 1:5$) (1months) (N=105)	100 (97 to 100)			
5/99 (hSBA $\geq 1:5$) (1months) (N= 103)	99 (95 to 100)			
NZ98/254 (hSBA $\geq 1:5$) (1months) (N= 108)	98 (93 to 100)			
M10713 (hSBA $\geq 1:5$) (1months) (N= 100)	97 (91 to 99)			
H44/76-SL (hSBA $\geq 1:5$) (6months) (N=104)	93 (87 to 97)			
5/99 (hSBA $\geq 1:5$) (6months) (N= 104)	96 (90 to 99)			
NZ98/254 (hSBA $\geq 1:5$) (6months) (N= 104)	18 (11 to 27)			
M10713 (hSBA $\geq 1:5$) (6months) (N= 104)	70 (60 to 79)			
H44/76-SL (hSBA $\geq 1:8$) (1months) (N=105)	100 (97 to 100)			
5/99 (hSBA $\geq 1:8$) (1months) (N= 103)	99 (95 to 100)			
NZ98/254 (hSBA $\geq 1:8$) (1months) (N= 108)	96 (91 to 99)			
M10713 (hSBA $\geq 1:8$) (1months) (N= 100)	95 (89 to 98)			
H44/76-SL (hSBA $\geq 1:8$) (6months) (N=104)	88 (80 to 93)			
5/99 (hSBA $\geq 1:8$) (6months) (N= 104)	96 (90 to 99)			
NZ98/254 (hSBA $\geq 1:8$) (6months) (N= 104)	12 (6 to 19)			
M10713 (hSBA $\geq 1:8$) (6months) (N= 104)	52 (42 to 62)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with fourfold increases in hSBA to assess antibody response at 1 month post two catch-up doses of rMenB+OMV NZ administered to naive children at 24 and 26 months of age

End point title	Percentage of subjects with fourfold increases in hSBA to assess antibody response at 1 month post two catch-up doses of rMenB+OMV NZ administered to naive children at 24 and 26 months of age ^[13]
-----------------	---

End point description:

To assess the immunogenicity in terms of percentage of subjects with fourfold increases in hSBA titers at 1 month post two catch-up doses of rMenB+OMV NZ in children previously administered to naive children at 24 and 26 months of age against 4 strains.

Analysis was done on MITT population (Secondary).

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

End point timeframe:

1 month post two catch-up doses versus prevaccination

Notes:

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

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

End point values	B_24_26			
Subject group type	Reporting group			
Number of subjects analysed	108			
Units: Percentage of subjects				
geometric mean (confidence interval 95%)				
H44/76-SL (N=105)	100 (97 to 100)			
5/99 (N= 101)	99 (95 to 100)			
NZ98/254 (N=108)	96 (91 to 99)			
M10713 (N= 99)	85 (76 to 91)			

Statistical analyses

No statistical analyses for this end point

Secondary: GMCs to assess antibody response at 1 month and 6 month post two catch-up doses of rMenB+OMV NZ administered to naive children at 24 and 26 months of age against 287-953 strain.

End point title	GMCs to assess antibody response at 1 month and 6 month post two catch-up doses of rMenB+OMV NZ administered to naive children at 24 and 26 months of age against 287-953 strain. ^[14]
-----------------	---

End point description:

To assess the immunogenicity in terms of GMCs to assess through antibody response at 1 month and 6 month post two catch-up doses of rMenB+OMV NZ administered to naive children at 24 and 26 months of age against 287-953 strain.

Analysis was done on MITT population (Secondary).

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

End point timeframe:

1 month and 6 months post two catch-up doses

Notes:

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

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

End point values	B_24_26			
Subject group type	Reporting group			
Number of subjects analysed	112			
Units: Concentration				
geometric mean (confidence interval 95%)				
287-953 strain (1 month, N=108)	5448 (4630 to 6411)			
287-953 strain (6 months, N=105)	383 (319 to 459)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting solicited local and systemic AEs after receiving a booster (3rd) dose of rMenB+OMV NZ administered at 1year after 2 catch-up doses of rMenB+OMV NZ, previously administered at either 12 & 14 or 13 & 15 months of age in V72P13E1

End point title	Number of subjects reporting solicited local and systemic AEs after receiving a booster (3rd) dose of rMenB+OMV NZ administered at 1year after 2 catch-up doses of rMenB+OMV NZ, previously administered at either 12 & 14 or 13 & 15 months of age in V72P13E1 ^[15]
-----------------	---

End point description:

To assess the safety and tolerability by reporting solicited local and systemic AEs of a booster (third) dose of rMenB+OMV NZ administered at one year after two catch-up doses of rMenB+OMV NZ, previously administered to children at either 12 and 14 or 13 and 15 months of age in study V72P13E1. The analysis was done on safety subset.

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

End point timeframe:

Up to 7 days after any 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: All safety analyses were run in the safety population.

EudraCT

End point values	B13_15_27	B12_14_26		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	67	18		
Units: Number of Subjects				
Any Local	64	16		
Tenderness (N=67,17)	63	16		
Erythema (N=67,17)	47	13		
Induration (N=67,17)	37	9		
Swelling (N=67,17)	35	9		
Any Systemic	53	15		
Change Eat. Habits (N=67,17)	25	9		
Sleepiness (N=67,17)	22	7		
Vomiting (N=67,17)	4	0		
Diarrhoea (N=67,17)	4	1		
Irritability (N=67,17)	40	14		
Unusual Crying (N=67,17)	16	5		
Rash (N=67,17)	1	0		
Fever (≥ 38C)	22	6		
Temperature (≥ 40 C) (N=67,17)	0	0		
Medical Attend. Fever (N=67,17)	0	0		

Antipyr. Med. Used Prev. (N=67,17)	12	5		
Antipyr. Med. Used Trt. (N=67,17)	20	6		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Reporting Unsolicited AEs after receiving a booster (3rd) dose of rMenB+OMV NZ administered at 1 year after 2 catch-up doses of rMenB+OMV NZ, previously administered to children at either 12 & 14 or 13 & 15 months of age in V72P13E2

End point title	Number of Subjects Reporting Unsolicited AEs after receiving a booster (3rd) dose of rMenB+OMV NZ administered at 1 year after 2 catch-up doses of rMenB+OMV NZ, previously administered to children at either 12 & 14 or 13 & 15 months of age in V72P13E2 ^[16]
-----------------	---

End point description:

To assess the safety and tolerability in terms of number of subjects reporting unsolicited AEs of a booster (third) dose of rMenB+OMV NZ administered at one year after two catch-up doses of rMenB+OMV NZ, previously administered to children at either 12 and 14 or 13 and 15 months of age in study V72P13E1.

The analysis was done on safety subset.

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

End point timeframe:

Up to 7 days after any 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: All safety analyses were run in the safety population.

EudraCT

End point values	B13_15_27	B12_14_26		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	67	18		
Units: Number of Subjects				
Any AE	45	10		
Serious AEs	2	1		
At least possibly related SAEs	0	0		
AEs leading to withdrawal	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting solicited local and systemic AEs after two catch-up doses of rMenB+OMV NZ administered to naive children at 24 and 26 months of age.

End point title	Number of subjects reporting solicited local and systemic AEs after two catch-up doses of rMenB+OMV NZ administered to
-----------------	--

End point description:

To assess the safety and tolerability by reporting solicited local and systemic AEs of two catch-up doses of rMenB+OMV NZ administered to naive children at 24 and 26 months of age.

The analysis was done on safety subset.

End point type

Secondary

End point timeframe:

Up to 7 days after any 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: All safety analyses were run in the safety population.

EudraCT

End point values	B_24_26			
Subject group type	Reporting group			
Number of subjects analysed	112			
Units: Number of subjects)				
Any Local	110			
Tenderness	109			
Erythema	103			
Induration	75			
Swelling	58			
Any Systemic	98			
Change Eat. Habits	53			
Sleepiness	70			
Vomiting	14			
Diarrhea	23			
Irritability	84			
Unusual Crying	47			
Rash	14			
Fever ($\geq 38^{\circ}\text{C}$)	44			
Temperature ($\geq 40^{\circ}\text{C}$)	1			
Medical Attend. Fever	2			
Antipyr. Med. Used Prev	33			
Antipyr. Med. Used Trt	38			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Reporting Unsolicited Adverse Events after receiving two catch-up doses of rMenB+OMV NZ administered to naive children at 24 and 26 months of age.

End point title

Number of Subjects Reporting Unsolicited Adverse Events after receiving two catch-up doses of rMenB+OMV NZ administered to naive children at 24 and 26 months of age.^[18]

End point description:

To assess the safety and tolerability in terms of number of subjects reporting unsolicited adverse events after receiving two catch-up doses of rMenB+OMV NZ administered to naive children at 24 and 26 months of age.

The analysis was done on safety subset.

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

End point timeframe:

Up to 7 days after any vaccination

Notes:

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

Justification: All safety analyses were run in the safety population.

EudraCT

End point values	B_24_26			
Subject group type	Reporting group			
Number of subjects analysed	112			
Units: Number of Subjects				
Any AE	96			
Serious AEs	6			
At least possibly related SAEs	0			
AEs leading to withdrawal	1			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Throughout the study (solicited and unsolicited from Day 1 to Day 209)

Adverse event reporting additional description:

Any solicited and unsolicited adverse events were reported up to day 7 post vaccination. Unsolicited SAE, medically attended AEs, AEs leading to withdrawal from the study were collected from day 1 through day.

Assessment type	Non-systematic
-----------------	----------------

Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	17.1
--------------------	------

Reporting groups

Reporting group title	B13_15_27
-----------------------	-----------

Reporting group description:

Subjects assessed for safety and tolerability after receiving a booster (third) dose of rMenB+OMV NZ at one year after two catch-up doses of rMenB+OMV NZ, previously administered to children at 13 and 15 months of age.

Reporting group title	B24_26
-----------------------	--------

Reporting group description:

Subjects assessed for safety and tolerability after two catch-up doses of rMenB+OMV NZ administered to naive children at 24 and 26 months of age.

Reporting group title	B12_14_26
-----------------------	-----------

Reporting group description:

Subjects assessed for safety and tolerability after receiving a booster (third) dose of rMenB+OMV NZ at one year after two catch-up doses of rMenB+OMV NZ, previously administered to children at either 12 and 14 months of age.

Serious adverse events	B13_15_27	B24_26	B12_14_26
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 67 (2.99%)	6 / 112 (5.36%)	1 / 18 (5.56%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cholesteatoma			
subjects affected / exposed	0 / 67 (0.00%)	1 / 112 (0.89%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Enteritis			

subjects affected / exposed	0 / 67 (0.00%)	1 / 112 (0.89%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Adenoidal Hypertrophy			
subjects affected / exposed	0 / 67 (0.00%)	1 / 112 (0.89%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 67 (1.49%)	1 / 112 (0.89%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngitis			
subjects affected / exposed	1 / 67 (1.49%)	0 / 112 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oral Herpes			
subjects affected / exposed	0 / 67 (0.00%)	0 / 112 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis Media			
subjects affected / exposed	0 / 67 (0.00%)	1 / 112 (0.89%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia Respiratory Syncytial Viral			
subjects affected / exposed	0 / 67 (0.00%)	1 / 112 (0.89%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Diabetes Mellitus			

subjects affected / exposed	0 / 67 (0.00%)	1 / 112 (0.89%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	B13_15_27	B24_26	B12_14_26
Total subjects affected by non-serious adverse events			
subjects affected / exposed	67 / 67 (100.00%)	110 / 112 (98.21%)	18 / 18 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Somnolence			
subjects affected / exposed	22 / 67 (32.84%)	70 / 112 (62.50%)	7 / 18 (38.89%)
occurrences (all)	22	109	7
Nervous system disorders			
Speech Disorder Developmental			
subjects affected / exposed	0 / 67 (0.00%)	0 / 112 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Crying			
subjects affected / exposed	16 / 67 (23.88%)	47 / 112 (41.96%)	5 / 18 (27.78%)
occurrences (all)	17	70	5
Induration			
subjects affected / exposed	1 / 67 (1.49%)	4 / 112 (3.57%)	1 / 18 (5.56%)
occurrences (all)	1	4	1
Injection Site Erythema			
subjects affected / exposed	47 / 67 (70.15%)	103 / 112 (91.96%)	13 / 18 (72.22%)
occurrences (all)	52	177	14
Injection Site Induration			
subjects affected / exposed	37 / 67 (55.22%)	75 / 112 (66.96%)	9 / 18 (50.00%)
occurrences (all)	54	156	12
Injection Site Pain			
subjects affected / exposed	63 / 67 (94.03%)	109 / 112 (97.32%)	16 / 18 (88.89%)
occurrences (all)	68	208	16
Injection Site Swelling			

subjects affected / exposed occurrences (all)	35 / 67 (52.24%) 39	58 / 112 (51.79%) 83	9 / 18 (50.00%) 11
Pyrexia subjects affected / exposed occurrences (all)	22 / 67 (32.84%) 23	46 / 112 (41.07%) 61	6 / 18 (33.33%) 6
Tenderness subjects affected / exposed occurrences (all)	1 / 67 (1.49%) 1	0 / 112 (0.00%) 0	1 / 18 (5.56%) 1
Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all)	1 / 67 (1.49%) 1	2 / 112 (1.79%) 2	1 / 18 (5.56%) 1
Diarrhoea subjects affected / exposed occurrences (all)	5 / 67 (7.46%) 5	24 / 112 (21.43%) 28	1 / 18 (5.56%) 2
Vomiting subjects affected / exposed occurrences (all)	4 / 67 (5.97%) 4	15 / 112 (13.39%) 17	0 / 18 (0.00%) 0
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	3 / 67 (4.48%) 3	14 / 112 (12.50%) 18	0 / 18 (0.00%) 0
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all)	1 / 67 (1.49%) 1	18 / 112 (16.07%) 20	0 / 18 (0.00%) 0
Psychiatric disorders Eating Disorder subjects affected / exposed occurrences (all)	25 / 67 (37.31%) 26	53 / 112 (47.32%) 80	9 / 18 (50.00%) 9
Irritability subjects affected / exposed occurrences (all)	40 / 67 (59.70%) 43	84 / 112 (75.00%) 140	14 / 18 (77.78%) 14
Infections and infestations Bronchitis			

subjects affected / exposed	4 / 67 (5.97%)	14 / 112 (12.50%)	1 / 18 (5.56%)
occurrences (all)	4	16	1
Conjunctivitis			
subjects affected / exposed	5 / 67 (7.46%)	16 / 112 (14.29%)	0 / 18 (0.00%)
occurrences (all)	5	19	0
Ear Infection			
subjects affected / exposed	1 / 67 (1.49%)	6 / 112 (5.36%)	0 / 18 (0.00%)
occurrences (all)	1	6	0
Exanthema Subitum			
subjects affected / exposed	0 / 67 (0.00%)	1 / 112 (0.89%)	1 / 18 (5.56%)
occurrences (all)	0	1	1
Gastroenteritis			
subjects affected / exposed	0 / 67 (0.00%)	6 / 112 (5.36%)	0 / 18 (0.00%)
occurrences (all)	0	6	0
Nasopharyngitis			
subjects affected / exposed	5 / 67 (7.46%)	9 / 112 (8.04%)	2 / 18 (11.11%)
occurrences (all)	5	10	2
Otitis Media			
subjects affected / exposed	7 / 67 (10.45%)	18 / 112 (16.07%)	1 / 18 (5.56%)
occurrences (all)	9	23	1
Pharyngitis			
subjects affected / exposed	2 / 67 (2.99%)	9 / 112 (8.04%)	0 / 18 (0.00%)
occurrences (all)	2	10	0
Pneumonia			
subjects affected / exposed	0 / 67 (0.00%)	0 / 112 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Rhinitis			
subjects affected / exposed	2 / 67 (2.99%)	8 / 112 (7.14%)	0 / 18 (0.00%)
occurrences (all)	2	10	0
Upper Respiratory Tract Infection			
subjects affected / exposed	5 / 67 (7.46%)	20 / 112 (17.86%)	1 / 18 (5.56%)
occurrences (all)	6	29	2
Viral Infection			
subjects affected / exposed	7 / 67 (10.45%)	14 / 112 (12.50%)	1 / 18 (5.56%)
occurrences (all)	8	15	2

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 December 2010	To perform assessment of persistence data generated one year after the booster (fourth) dose of rMenB+OMV NZ (groups B246_12M12 and B246_12M13) and one year after the two catch-up doses of rMenB+OMV NZ (groups B13_15_27 and B12_14_26) with a comparison against baseline titers of naive subjects at 24 months of age (group B_24_26).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported