Clinical trial results:
A Phase 2, Open-Label, Single-Center, Extension Study Evaluating Antibody Persistence compared to Naïve Children and Safety, Tolerability and Immunogenicity of Booster Doses of Novartis rMenB±OMV NZ Vaccine in Healthy UK Children Who Previously Received One or Four Doses of the Novartis Vaccine as Infants in Study V72P6.

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

Summary

EudraCT number	2009-013054-33
Trial protocol	GB
Global end of trial date	22 May 2012

Results information

Result version number	v2 (current)
This version publication date	10 June 2016
First version publication date	01 November 2014
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	V72P6E1

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01027351
WHO universal trial number (UTN)	-

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

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

1901/2006 apply to this trial?	

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	10 June 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	22 May 2012
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The present study, V72P6E1, is an extension of V72P6. The primary objective of this extension study will be to explore antibody persistence at approximately 40 months of age in subjects who received rMenB or rMenB+OMV NZ at 2, 4, 6 and 12 months of age in parent study V72P6.

Protection of trial subjects:

Study vaccines were not administered to individuals with known hypersensitivity to any component of the vaccines.
An oral temperature ≥38.0°C (≥100.4°F) or serious active infection was a reason for delaying vaccination.
Standard immunization practices were observed and care was taken to administer the injection intramuscularly. As with all injectable vaccines, appropriate medical treatment and supervision was readily available in case of rare anaphylactic reactions following administration of the study vaccine. Epinephrine 1:1000 and diphenhydramine was available in case of any anaphylactic reactions. Care was taken to ensure that the vaccine is not injected into a blood vessel.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 January 2010
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	United Kingdom: 163
Worldwide total number of subjects	163
EEA total number of subjects	163

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)	0
Children (2-11 years)	163
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 recruited from one centre in the United Kingdom.

Pre-assignment

Screening details:

All subjects were included in the trial.

Pre-assignment period milestones

Number of subjects started	163
Number of subjects completed	163

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	5rMenB

Arm description:

Subjects who had received four doses of rMenB vaccine (at 2,4,6 and 12 months of age) in the parent study were administered a fifth dose of rMenB vaccine, at 40 months of age in the present study.

Arm type	Experimental
Investigational medicinal product name	Meningococcal (group B) multicomponent recombinant adsorbed vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects were administered 1 dose of 0.5 millilitres.

Arm title	5rMenB+OMV NZ

Arm description:

Subjects who had received four doses of rMenB +OMV NZ vaccine (at 2,4,6 and 12 months of age) in the parent study were administered a fifth dose of rMenB +OMV NZ vaccine, at 40 months of age in the present study.

Arm type	Experimental
Investigational medicinal product name	Meningococcal (group B) multicomponent recombinant adsorbed vaccine plus Outer Membrane Vesicles New Zealand (OMV NZ)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects were administered 1 dose of 0.5 millilitres.

Arm title	3rMenB

Arm description:

Subjects who had previously received one dose of rMenB vaccine (at 12 months of age) were administered two doses of rMenB vaccine, at 40 and 42 months of age in the present study.

Arm type	Experimental
Investigational medicinal product name	Meningococcal (group B) multicomponent recombinant adsorbed vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects were administered 2 doses of 0.5 millilitres.

Arm title	3rMenB+OMV NZ

Arm description:

Subjects who had previously received one dose of rMenB +OMV NZ vaccine (at 12 months of age) were administered two doses of rMenB +OMV NZ vaccine, at 40 and 42 months of age in the present study.

Arm type	Experimental
Investigational medicinal product name	Meningococcal (group B) multicomponent recombinant adsorbed vaccine plus Outer Membrane Vesicles New Zealand (OMV NZ)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects were administered 2 doses of 0.5 millilitres.

Arm title	Naive_4042

Arm description:

Vaccine-naive subjects who received two catch -up doses of rMenB+OMV NZ vaccine at 40 and 42 months of age in the present study.

Arm type	Experimental
Investigational medicinal product name	Meningococcal (group B) multicomponent recombinant adsorbed vaccine plus Outer Membrane Vesicles New Zealand (OMV NZ)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects were administered 2 doses of 0.5 millilitres.

Arm title	Naive_6062

Arm description:

Vaccine-naive subjects who received two catch-up doses of rMenB+OMV NZ vaccine at 60 and 62 months of age in the present study.

Arm type	Experimental
Investigational medicinal product name	Meningococcal (group B) multicomponent recombinant adsorbed vaccine plus OMV NZ
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects were administered 2 doses of 0.5 millilitres.

Number of subjects in period 1	5rMenB	5rMenB+OMV NZ	3rMenB
Started	29	19	14
Completed	26	18	13
Not completed	3	1	1
Consent withdrawn by subject	1	-	1
Lost to follow-up	1	1	-
inappropriate enrollment	-	-	-
Protocol deviation	1	-	-

Number of subjects in period 1	3rMenB+OMV NZ	Naive_4042	Naive_6062
Started	8	43	50
Completed	6	32	45
Not completed	2	11	5
Consent withdrawn by subject	-	3	5
Lost to follow-up	1	6	-
inappropriate enrollment	-	1	-
Protocol deviation	1	1	-

Baseline characteristics

Reporting groups	
Reporting group title	5rMenB
Reporting group description:	
Subjects who had received four doses of rMenB vaccine (at 2,4,6 and 12 months of age) in the parent study were administered a fifth dose of rMenB vaccine, at 40 months of age in the present study.	
Reporting group title	5rMenB+OMV NZ
Reporting group description:	
Subjects who had received four doses of rMenB +OMV NZ vaccine (at 2,4,6 and 12 months of age) in the parent study were administered a fifth dose of rMenB +OMV NZ vaccine, at 40 months of age in the present study.	
Reporting group title	3rMenB
Reporting group description:	
Subjects who had previously received one dose of rMenB vaccine (at 12 months of age) were administered two doses of rMenB vaccine, at 40 and 42 months of age in the present study.	
Reporting group title	3rMenB+OMV NZ
Reporting group description:	
Subjects who had previously received one dose of rMenB +OMV NZ vaccine (at 12 months of age) were administered two doses of rMenB +OMV NZ vaccine, at 40 and 42 months of age in the present study.	
Reporting group title	Naive_4042
Reporting group description:	
Vaccine-naive subjects who received two catch -up doses of rMenB+OMV NZ vaccine at 40 and 42 months of age in the present study.	
Reporting group title	Naive_6062
Reporting group description:	
Vaccine-naive subjects who received two catch-up doses of rMenB+OMV NZ vaccine at 60 and 62 months of age in the present study.	

Reporting group values	5rMenB	5rMenB+OMV NZ	3rMenB
Number of subjects	29	19	14
Age categorical			
Units: Subjects			
Age continuous			
Units: months			
arithmetic mean	41.4	41.8	41.4
standard deviation	± 1.5	± 1.4	± 1.5
Gender categorical			
Units: Subjects			
Female	17	9	5
Male	12	10	9

Reporting group values	3rMenB+OMV NZ	Naive_4042	Naive_6062
Number of subjects	8	43	50
Age categorical			
Units: Subjects			

Age continuous Units: months			
arithmetic mean	40.4	41.8	61.3
standard deviation	± 0.7	± 1.7	± 0.9
Gender categorical Units: Subjects			
Female	3	23	27
Male	5	20	23

Reporting group values	Total		
Number of subjects	163		
Age categorical Units: Subjects			

Age continuous Units: months			
arithmetic mean			
standard deviation	-		
Gender categorical Units: Subjects			
Female	84		
Male	79		

Subject analysis sets

Subject analysis set title	MITT – 40 months of age antibody persistence population
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

MITT – 40 months of age antibody persistence population (groups 5rMenB, 5rMenB+OMV, 3rMenB, 3rMenB+OMV, Naive_4042). All subjects in the all enrolled population who:
provided an evaluable serum sample at 40 months of age, (ie at visit 1 of V72P6E1 for groups 5rMenB, 5rMenB+OMV, 3rMenB, 3rMenB+OMV and Naive_4042).

Subject analysis set title	MITT – 60 Months of Age Antibody Persistence population
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

MITT – 60 Months of Age Antibody Persistence population (5rMenB, 5rMenB+OMV NZ, 3rMenB, 3rMenB+OMV NZ, Naive_4042, Naive_6062). All subjects in the All Enrolled Set who provide an evaluable serum sample at 60 Months of Age (Visit 3 of V72P6E1 for groups 5rMenB and 5rMenB+OMV NZ, Visit 5 for Groups 3rMenB, 3rMenB+OMV NZ, Naive_4042, Visit 1 for Group Naive_6062).

Subject analysis set title	MITT – Booster Response population
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

MITT – Booster Response population (Groups 5rMenB, 5rMenB+OMV, 3rMenB, 3rMenB+OMV, Naive_4042, Naive_6062). For Groups 5rMenB, 5rMenB+OMV, 3rMenB, 3rMenB+OMV, Naive_4042, all subjects in the All enrolled set who:
▫ receive a study vaccination in the present V72P6E1 study; and
▫ provide an evaluable serum sample either, at one month after the (first) (booster) dose (Visit 2) or at one month after the second (booster) dose (for Groups 3rMenB, 3rMenB+OMV, Naive_4042 Visit 4);
For Group Naive_6062, all subjects in the All enrolled set who provide an evaluable serum sample at 60 Months of Age (Visit 1).

Subject analysis set title	Exposed set
Subject analysis set type	Safety analysis

Subject analysis set description:

All enrolled subjects who actually receive a rMenB + OMV vaccination

Subject analysis set title	Safety Set
Subject analysis set type	Safety analysis

Subject analysis set description:

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

Subject analysis set title	MITT – Two Dose Catch Up Schedule population
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

MITT – Two Dose Catch Up Schedule population (Groups Naive_4042 and Naive_6062). All subjects in the All enrolled set who:
▫ received a study vaccination in the present V72P6E1 study; and
▫ provided an evaluable serum sample either, at one month after the first dose (Visit 2 for Naive_4042 only) or at one month after the second dose (Visit 4 for Group Naive_4042 and Visit 3 for Group Naive_6062).

Reporting group values	MITT – 40 months of age antibody persistence population	MITT – 60 Months of Age Antibody Persistence population	MITT – Booster Response population
Number of subjects	108	134	160
Age categorical Units: Subjects			
Age continuous Units: months			
arithmetic mean	41.5	48.4	47.7
standard deviation	± 1.6	± 9.6	± 9.3
Gender categorical Units: Subjects			
Female	54	68	83
Male	54	66	77

Reporting group values	Exposed set	Safety Set	MITT – Two Dose Catch Up Schedule population
Number of subjects	162	162	152
Age categorical Units: Subjects			
Age continuous Units: months			
arithmetic mean	47.6	47.6	47
standard deviation	± 9.3	± 9.3	± 9
Gender categorical Units: Subjects			
Female	84	84	80
Male	78	78	72

End points

End points reporting groups

Reporting group title	5rMenB
Reporting group description:	
Subjects who had received four doses of rMenB vaccine (at 2,4,6 and 12 months of age) in the parent study were administered a fifth dose of rMenB vaccine, at 40 months of age in the present study.	
Reporting group title	5rMenB+OMV NZ
Reporting group description:	
Subjects who had received four doses of rMenB +OMV NZ vaccine (at 2,4,6 and 12 months of age) in the parent study were administered a fifth dose of rMenB +OMV NZ vaccine, at 40 months of age in the present study.	
Reporting group title	3rMenB
Reporting group description:	
Subjects who had previously received one dose of rMenB vaccine (at 12 months of age) were administered two doses of rMenB vaccine, at 40 and 42 months of age in the present study.	
Reporting group title	3rMenB+OMV NZ
Reporting group description:	
Subjects who had previously received one dose of rMenB +OMV NZ vaccine (at 12 months of age) were administered two doses of rMenB +OMV NZ vaccine, at 40 and 42 months of age in the present study.	
Reporting group title	Naive_4042
Reporting group description:	
Vaccine-naive subjects who received two catch -up doses of rMenB+OMV NZ vaccine at 40 and 42 months of age in the present study.	
Reporting group title	Naive_6062
Reporting group description:	
Vaccine-naive subjects who received two catch-up doses of rMenB+OMV NZ vaccine at 60 and 62 months of age in the present study.	
Subject analysis set title	MITT – 40 months of age antibody persistence population
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
MITT – 40 months of age antibody persistence population (groups 5rMenB, 5rMenB+OMV, 3rMenB, 3rMenB+OMV, Naive_4042). All subjects in the all enrolled population who: provided an evaluable serum sample at 40 months of age, (ie at visit 1 of V72P6E1 for groups 5rMenB, 5rMenB+OMV, 3rMenB, 3rMenB+OMV and Naive_4042).	
Subject analysis set title	MITT – 60 Months of Age Antibody Persistence population
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
MITT – 60 Months of Age Antibody Persistence population (5rMenB, 5rMenB+OMV NZ, 3rMenB, 3rMenB+OMV NZ, Naive_4042, Naive_6062). All subjects in the All Enrolled Set who provide an evaluable serum sample at 60 Months of Age (Visit 3 of V72P6E1 for groups 5rMenB and 5rMenB+OMV NZ, Visit 5 for Groups 3rMenB, 3rMenB+OMV NZ, Naive_4042, Visit 1 for Group Naive_6062).	
Subject analysis set title	MITT – Booster Response population
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
MITT – Booster Response population (Groups 5rMenB, 5rMenB+OMV, 3rMenB, 3rMenB+OMV, Naive_4042, Naive_6062). For Groups 5rMenB, 5rMenB+OMV, 3rMenB, 3rMenB+OMV, Naive_4042, all subjects in the All enrolled set who: ▫ receive a study vaccination in the present V72P6E1 study; and ▫ provide an evaluable serum sample either, at one month after the (first) (booster) dose (Visit 2) or at one month after the second (booster) dose (for Groups 3rMenB, 3rMenB+OMV, Naive_4042 Visit 4); For Group Naive_6062, all subjects in the All enrolled set who provide an evaluable serum sample at 60 Months of Age (Visit 1).	
Subject analysis set title	Exposed set
Subject analysis set type	Safety analysis

Subject analysis set description:

All enrolled subjects who actually receive a rMenB + OMV vaccination

Subject analysis set title	Safety Set
Subject analysis set type	Safety analysis

Subject analysis set description:

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

Subject analysis set title	MITT – Two Dose Catch Up Schedule population
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

MITT – Two Dose Catch Up Schedule population (Groups Naive_4042 and Naive_6062). All subjects in the All enrolled set who:
▫ received a study vaccination in the present V72P6E1 study; and
▫ provided an evaluable serum sample either, at one month after the first dose (Visit 2 for Naive_4042 only) or at one month after the second dose (Visit 4 for Group Naive_4042 and Visit 3 for Group Naive_6062).

Primary: 1) Persistence of geometric mean antibody titers in children (who previously received 4 doses of Men B vaccine), at 40 months of age

End point title	1) Persistence of geometric mean antibody titers in children (who previously received 4 doses of Men B vaccine), at 40 months of age[1][2]

End point description:

Persistence of geometric mean titers (GMTs) against N.meningitidis B strains in children (at 40 months of age) who had previously received four doses of either rMenB or rMen+OMV NZ vaccines in parent study, are compared with the GMTs in vaccine-naïve children.

Analysis was done on the MITT – 40 months of age antibody persistence population.

End point type	Primary

End point timeframe:

28 months after last vaccination; Baseline for Naïve

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	5rMenB	5rMenB+OMV NZ	Naive_4042	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	29	17	40	
Units: Titers				
geometric mean (confidence interval 95%)				
H 44/76 strain	3.24 (2.33 to 4.52)	5.34 (3.47 to 8.23)	4.25 (3.22 to 5.6)	
5/99 strain (N=28, 17, 40)	5.11 (2.33 to 11)	28 (10 to 77)	1.11 (0.9 to 1.36)	
NZ 98/254 strain	1.09 (0.79 to 1.51)	2.77 (1.81 to 4.23)	1 (1 to 1)	
M10713 strain (N=28, 15, 40)	9.15 (5.01 to 17)	5.34 (2.35 to 12)	8.75 (5.22 to 15)	

Statistical analyses

No statistical analyses for this end point

Primary: 2) Percentage of subjects (who previously received 4 doses of Men B vaccine) with persisting serum bactericidal antibody titers ≥ 1: 4 and ≥ 1: 8 at 40 months of age

End point title	2) Percentage of subjects (who previously received 4 doses of Men B vaccine) with persisting serum bactericidal antibody titers ≥ 1: 4 and ≥ 1: 8 at 40 months of age[3][4]

End point description:

The percentages of subjects with persisting serum bactericidal antibodies (hSBA) titers ≥ 1:4 and ≥ 1:8, against N.meningitidis B strains at 40 months of age who had previously received four doses of either rMenB or rMen+OMV NZ vaccines in parent study are reported.
The serum bactericidal antibodies directed against serogroup B meningococci, are measured by human complement Serum Bactericidal Assay (hSBA).

Analysis was done on the MITT – 40 months of age antibody persistence population.

End point type	Primary

End point timeframe:

28 months after last vaccination; Baseline for Naïve

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	5rMenB	5rMenB+OMV NZ	Naive_4042	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	29	17	40	
Units: percentages of subjects				
number (confidence interval 95%)				
hSBA ≥1:4 (H44/76 strain)	45 (26 to 64)	65 (38 to 86)	63 (46 to 77)	
hSBA≥1:4 (5/99 strain)	43 (24 to 63)	76 (50 to 93)	3 (0.063 to 13)	
hSBA≥1:4 (NZ 98/254 strain)	3 (0.087 to 18)	41 (18 to 67)	0 (0 to 9)	
hSBA≥1:4 (M10713 strain)	68 (48 to 84)	67 (38 to 88)	68 (51 to 81)	
hSBA ≥1:8 (H44/76 strain)	14 (4 to 32)	35 (14 to 62)	30 (17 to 47)	
hSBA≥1:8 (5/99 strain)	43 (24 to 63)	76 (50 to 93)	3 (0.063 to 13)	
hSBA≥1:8 (NZ 98/254 strain)	0 (0 to 12)	24 (7 to 50)	0 (0 to 9)	
hSBA≥1:8 (M10713 strain)	61 (41 to 78)	40 (16 to 68)	45 (29 to 62)	

Statistical analyses

No statistical analyses for this end point

Primary: 3) Number of subjects reporting solicited adverse events after receiving one or two booster doses of rMen B or rMenB+OMV NZ vaccine at 40 months of age.

End point title	3) Number of subjects reporting solicited adverse events after receiving one or two booster doses of rMen B or rMenB+OMV NZ vaccine at 40 months of age.[5][6]

End point description:

The safety and tolerability of one or two booster doses of rMen B or rMenB+OMV NZ vaccine administered at 40 months of age in children who had previously received one or four doses of the same vaccine as infants in parent study is assessed in terms of number of subjects with solicited local and systemic reactions following vaccination.

Analysis was done on the safety population, ie, all subjects in the exposed set who provide post-baseline safety data.

End point type	Primary

End point timeframe:

Day 1-7 after booster 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 safety 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 safety objective.

End point values	5rMenB	5rMenB+OMV NZ	3rMenB	3rMenB+OMV NZ
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	19	14	8
Units: Number of participants				
Local	28	19	14	8
Injection-site pain	17	14	8	8
Injection-site erythema	28	19	14	8
Injection-site swelling	13	5	9	4
Injection-site induration	14	9	8	6
Systemic	19	13	11	8
Changes in eating habits	5	10	5	4
Sleepiness	13	12	8	6
Vomiting	1	3	3	0
Diarrhea	3	1	3	1
Irritability	14	10	9	8
Headache	1	0	2	1
Arthralgia	0	6	4	4
Rash	3	0	2	1
Fever (≥38°C)	1	1	4	0
Other	10	12	5	7
Antipyretic preventive medication used	10	12	3	7
Antipyretic treatment medication used	1	2	4	0
Medically attended fever	0	0	1	0

Statistical analyses

No statistical analyses for this end point

Secondary: 4) Persistence of geometric mean antibody titers in children (who previously received one dose of Men B vaccine), at 40 months of age

End point title	4) Persistence of geometric mean antibody titers in children (who previously received one dose of Men B vaccine), at 40 months of age[7]

End point description:

Persisting GMTs against N.meningitidis B strains in children (at 40 months of age) who had previously received one dose of either rMenB or rMen+OMV NZ vaccines in parent study, are compared with the GMTs in vaccine-naïve children.

Analysis was done on the MITT – 40 months of age antibody persistence population.

End point type	Secondary

End point timeframe:

28 months after vaccination; baseline for Naïve

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	3rMenB	3rMenB+OMV NZ	Naive_4042	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	14	8	40	
Units: Titers				
geometric mean (confidence interval 95%)				
H44/76 strain	3.59 (1.8 to 7.15)	3.47 (1.39 to 8.64)	4.25 (3.22 to 5.6)	
5/99 strain	9.57 (3.88 to 24)	1 (0.3 to 3.3)	1.11 (0.9 to 1.36)	
NZ 98/254 strain	1.23 (0.96 to 1.57)	1 (0.72 to 1.38)	1 (1 to 1)	
M10713 strain (N=13, 8, 40)	3.26 (1.49 to 7.11)	3 (1.11 to 8.11)	8.75 (5.22 to 15)	

Statistical analyses

No statistical analyses for this end point

Secondary: 5) Percentage of Subjects (Who Had Previously Received One Dose of Men B Vaccine) With Persisting Serum Bactericidal Antibody Titers ≥ 1:4 and ≥ 1:8 at 40 Months of Age

End point title	5) Percentage of Subjects (Who Had Previously Received One Dose of Men B Vaccine) With Persisting Serum Bactericidal Antibody Titers ≥ 1:4 and ≥ 1:8 at 40 Months of Age[8]

End point description:

The percentages of subjects with persisting hSBA titers ≥ 1: 4 and ≥ 1:8, against N.meningitidis B strains at 40 months of age who had previously received one dose of either rMenB or rMen+OMV NZ vaccines in parent study are reported.

Analysis was done on the MITT – 40 months of age antibody persistence population.

End point type	Secondary

End point timeframe:

28 months after vaccination; baseline for naïve

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	3rMenB	3rMenB+OMV NZ	Naive_4042	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	14	8	40	
Units: Percentages of subjects				
number (confidence interval 95%)				
hSBA ≥1:4 (H44/76 strain)	57 (29 to 82)	38 (9 to 76)	63 (46 to 77)	
hSBA≥1:4 (5/99 strain)	57 (29 to 82)	0 (0 to 37)	3 (0.063 to 13)	
hSBA≥1:4 (NZ 98/254 strain)	7 (0 to 34)	0 (0 to 37)	0 (0 to 9)	
hSBA≥1:4 (M10713 strain; N=13, 8, 40)	54 (25 to 81)	25 (3 to 65)	68 (51 to 81)	
hSBA ≥1:8 (H44/76 strain)	7 (0 to 34)	13 (0 to 53)	30 (17 to 47)	
hSBA≥1:8 (5/99 strain)	43 (18 to 71)	0 (0 to 37)	3 (0.063 to 13)	
hSBA≥1:8 (NZ 98/254 strain)	0 (0 to 23)	0 (0 to 37)	0 (0 to 9)	
hSBA≥1:8 (M10713 strain; N=13, 8, 40)	15 (2 to 45)	13 (0 to 53)	45 (29 to 62)	

Statistical analyses

No statistical analyses for this end point

Secondary: 6) Geometric Mean Antibody Titers in Children (Who Previously Received 4 Doses of Men B Vaccine), After Receiving a Booster Dose of rMenB or rMenB+OMV NZ Vaccine at 40 Months of Age

End point title	6) Geometric Mean Antibody Titers in Children (Who Previously Received 4 Doses of Men B Vaccine), After Receiving a Booster Dose of rMenB or rMenB+OMV NZ Vaccine at 40 Months of Age[9]

End point description:

The GMTs against N.meningitidis B strains in children (who had previously received four doses MenB vaccine in parent study) after a single booster dose of rMenB or rMenB+OMV NZ vaccine given at 40 months of age, are compared with the antibody titers following one catch-up dose rMenB+OMV NZ vaccine given at 40 months to vaccine-naive subjects.

Analysis was done on the MITT – Booster Response population.

End point type	Secondary

End point timeframe:

1 month post- booster/ dose 1 for Naïve

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	5rMenB	5rMenB+OMV NZ	Naive_4042	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	29	19	38	
Units: Titers				
geometric mean (confidence interval 95%)				
H44/76 strain	99 (67 to 145)	89 (56 to 141)	12 (7.96 to 19)	
5/99 strain (N=28, 18, 38)	778 (448 to 1349)	1708 (859 to 3396)	22 (12 to 40)	
NZ 98/254 strain	1.64 (0.95 to 2.85)	47 (24 to 91)	7.73 (4.62 to 13)	

M10713 strain (N=28, 18, 38)	38 (24 to 59)	39 (22 to 67)	11 (6.7 to 19)	

Statistical analyses

No statistical analyses for this end point

Secondary: 7) Percentage of subjects (who previously received 4 doses of Men B vaccine) with serum bactericidal antibody titers ≥1:4 and ≥1: 8 after receiving a booster dose of either rMenB or rMenB+OMV NZ vaccine at 40 months of age

End point title	7) Percentage of subjects (who previously received 4 doses of Men B vaccine) with serum bactericidal antibody titers ≥1:4 and ≥1: 8 after receiving a booster dose of either rMenB or rMenB+OMV NZ vaccine at 40 months of age[10]

End point description:

The percentages of subjects (who had previously received four doses MenB vaccine in parent study) with hSBA titers ≥ 1:4 and ≥ 1:8, against N.meningitidis B strains after receiving a single booster dose of either rMenB or rMen+OMV NZ vaccines at 40 months of age are compared with hSBA responses following one catch-up dose of rMenB+OMV NZ vaccine given at 40 months in vaccine-naive subjects.

Analysis was done on the MITT – Booster Response population.

End point type	Secondary

End point timeframe:

1 month post- booster/ dose 1 for Naïve

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	5rMenB	5rMenB+OMV NZ	Naive_4042	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	28	19	38	
Units: Percentages of subjects				
number (confidence interval 95%)				
hSBA ≥1:4 (H44/76 strain)	100 (88 to 100)	100 (82 to 100)	89 (75 to 97)	
hSBA≥1:4 (5/99 strain)	100 (88 to 100)	100 (81 to 100)	76 (60 to 89)	
hSBA≥1:4 (NZ 98/254 strain)	14 (4 to 33)	89 (67 to 99)	66 (49 to 80)	
hSBA≥1:4 (M10713 strain)	96 (82 to 100)	94 (73 to 100)	76 (60 to 89)	
hSBA ≥1:8 (H44/76 strain)	96 (82 to 100)	100 (82 to 100)	63 (46 to 78)	
hSBA≥1:8 (5/99 strain)	100 (88 to 100)	100 (81 to 100)	71 (54 to 85)	
hSBA≥1:8 (NZ 98/254 strain)	11 (2 to 28)	89 (67 to 99)	58 (41 to 74)	
hSBA≥1:8 (M10713 strain)	89 (72 to 98)	94 (73 to 100)	61 (43 to 76)	

Statistical analyses

No statistical analyses for this end point

Secondary: 8) Percentage of subjects (who previously received 4 doses of Men B vaccine) with 4-fold increase in serum bactericidal antibody titers after receiving a booster dose of either rMenB or rMenB+OMV NZ vaccine at 40 months of age

End point title	8) Percentage of subjects (who previously received 4 doses of Men B vaccine) with 4-fold increase in serum bactericidal antibody titers after receiving a booster dose of either rMenB or rMenB+OMV NZ vaccine at 40 months of age[11]

End point description:

The percentages of subjects (who had previously received four doses MenB vaccine in parent study) showing a 4-fold increase in hSBA titers over baseline against N.meningitidis B strains, after receiving a booster dose of either rMenB or rMen+OMV NZ vaccines at 40 months of age are compared with hSBA responses following one catch-up dose of rMenB+OMV NZ vaccine given at 40 months in vaccine-naive subjects.

Baseline is defined as either the time that the (first) booster dose was given or the time of the first vaccination in this study.
Analysis was done on the MITT – Booster Response population.

End point type	Secondary

End point timeframe:

1 month post- booster/ dose 1 for Naïve

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	5rMenB	5rMenB+OMV NZ	Naive_4042	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	28	17	37	
Units: Percentages of subjects				
number (confidence interval 95%)				
H44/76 strain	89 (72 to 98)	94 (71 to 100)	41 (25 to 58)	
5/99 strain (N=27, 16, 37)	100 (87 to 100)	94 (70 to 100)	68 (50 to 82)	
NZ 98/254 strain	11 (2 to 28)	82 (57 to 96)	57 (39 to 73)	
M10713 strain (N=27, 15, 37)	41 (22 to 61)	67 (38 to 88)	14 (5 to 29)	

Statistical analyses

No statistical analyses for this end point

Secondary: 9) Geometric mean antibody titers in children after receiving two booster doses of either rMenB or rMenB+OMV NZ vaccine at 40 & 42 months of age

End point title	9) Geometric mean antibody titers in children after receiving two booster doses of either rMenB or rMenB+OMV NZ vaccine at 40 & 42 months of age[12]

End point description:

The GMTs against N.meningitidis B strains in children (who had previously received one dose MenB vaccine in parent study) after a two booster doses of either rMenB or rMenB+OMV NZ vaccine given at 40 & 42 months of age.

Analysis was done on the MITT – Booster Response population.

End point type	Secondary

End point timeframe:

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

End point values	3rMenB	3rMenB+OMV NZ	Naive_4042	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	8	38	
Units: Titers				
geometric mean (confidence interval 95%)				
H44/76 strain (dose 1; N=13, 7, 38)	94 (48 to 185)	76 (30 to 190)	12 (7.96 to 19)	
H44/76 strain (dose 2; N=13, 8, 36)	127 (81 to 198)	145 (82 to 255)	88 (66 to 117)	
5/99 strain (dose 1; N=13, 7, 38)	2379 (1164 to 4859)	509 (192 to 1348)	22 (12 to 40)	
5/99 strain (dose 2; N=13, 8, 36)	5240 (3082 to 8911)	2413 (1226 to 4747)	1019 (762 to 1362)	
NZ 98/254 strain (dose 1; N=13, 7, 38)	1.73 (0.86 to 3.48)	148 (57 to 384)	7.73 (4.62 to 13)	
NZ 98/254 strain (dose 2; N=13, 8, 36)	1.86 (0.89 to 3.88)	65 (25 to 165)	47 (31 to 72)	
M10713 strain (dose 1; N=13, 7, 38)	35 (18 to 68)	30 (12 to 74)	11 (6.7 to 19)	
M10713 strain (dose 2; N=12, 8, 36)	21 (9.25 to 47)	36 (13 to 98)	33 (22 to 51)	

Statistical analyses

No statistical analyses for this end point

Secondary: 10) Percentage of subjects with serum bactericidal antibody titers ≥1: 4 and ≥1: 8 after receiving two booster doses of either rMenB or rMenB+OMV NZ vaccine at 40 & 42 months of age

End point title	10) Percentage of subjects with serum bactericidal antibody titers ≥1: 4 and ≥1: 8 after receiving two booster doses of either rMenB or rMenB+OMV NZ vaccine at 40 & 42 months of age[13]

End point description:

The percentages of subjects (who had previously received one dose of MenB vaccine in parent study) with hSBA ≥ 1:4 and ≥ 1:8, against N.meningitidis B strains after receiving two booster doses of either rMenB or rMenB+OMV NZ vaccine at 40 & 42 months of age are reported.

Analysis was done on the MITT – Booster Response population.

End point type	Secondary

End point timeframe:

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

End point values	3rMenB	3rMenB+OMV NZ	Naive_4042	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	8	38	
Units: Percentage of subjects				
number (confidence interval 95%)				
H44/76 strain (≥1:4 – booster dose 1)	100 (75 to 100)	100 (59 to 100)	89 (75 to 100)	
H44/76 strain (≥1:4 – booster dose 2)	100 (75 to 100)	100 (63 to 100)	100 (90 to 100)	
H44/76 strain (≥1:8 – booster dose 1)	100 (75 to 100)	100 (59 to 100)	63 (46 to 78)	
H44/76 strain (≥1:8 – booster dose 2)	100 (75 to 100)	100 (63 to 100)	100 (90 to 100)	
5/99 strain (≥1:4 – booster dose 1)	100 (75 to 100)	100 (59 to 100)	76 (60 to 89)	
5/99 strain (≥1:4 – booster dose 2)	100 (75 to 100)	100 (63 to 100)	100 (90 to 100)	
5/99 strain (≥1:8 – booster dose 1)	100 (75 to 100)	100 (59 to 100)	71 (54 to 85)	
5/99 strain (≥1:8 – booster dose 2)	100 (75 to 100)	100 (63 to 100)	100 (90 to 100)	
NZ 98/254 strain (≥1:4 – booster dose 1)	15 (2 to 45)	100 (59 to 100)	66 (49 to 80)	
NZ 98/254 strain (≥1:4 – booster dose 2)	15 (2 to 45)	100 (63 to 100)	94 (81 to 99)	
NZ 98/254 strain (≥1:8 – booster dose 1)	15 (2 to 45)	100 (59 to 100)	58 (41 to 74)	
NZ 98/254 strain (≥1:8 – booster dose 2)	15 (2 to 45)	100 (63 to 100)	94 (81 to 99)	
M10713 strain (≥1:4 – booster dose 1)	100 (75 to 100)	86 (42 to 100)	76 (60 to 89)	
M10713 strain (≥1:4 – booster dose 2)	83 (52 to 98)	100 (63 to 100)	89 (74 to 97)	
M10713 strain (≥1:8 – booster dose 1)	85 (55 to 98)	86 (42 to 100)	61 (43 to 76)	
M10713 strain (≥1:8 – booster dose 2)	75 (43 to 95)	100 (63 to 100)	86 (71 to 95)	

Statistical analyses

No statistical analyses for this end point

Secondary: 11) Percentage of subjects with 4-fold increase in antibody titers after receiving two booster doses of either rMenB or rMenB+OMV NZ vaccine at 40 & 42 months of age

End point title	11) Percentage of subjects with 4-fold increase in antibody titers after receiving two booster doses of either rMenB or rMenB+OMV NZ vaccine at 40 & 42 months of age[14]

End point description:

The percentages of subjects (who had previously received one dose of MenB vaccine in parent study) displaying 4-fold increase in antibody titers over baseline against N.meningitidis B strains, after receiving two booster doses of either rMenB or rMenB+OMV NZ vaccine at 40 & 42 months of age are reported.

Analysis was done on the MITT – Booster Response population.

End point type	Secondary

End point timeframe:

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

End point values	3rMenB	3rMenB+OMV NZ	Naive_4042	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	8	37	
Units: Percentage of subjects				
geometric mean (confidence interval 95%)				
H44/76 strain (dose 1; N=13, 7, 37)	100 (75 to 100)	86 (42 to 100)	41 (25 to 58)	
5/99 strain (dose 1; N=13, 7, 37)	100 (75 to 100)	100 (59 to 100)	68 (50 to 82)	
NZ 98/254 strain (dose 1; N=13, 7, 37)	15 (2 to 45)	100 (59 to 100)	57 (39 to 73)	
M10713 strain (dose 1; N=12, 7, 37)	58 (28 to 85)	57 (18 to 90)	14 (5 to 29)	
H44/76 strain (dose 2; N=13, 8, 34)	100 (75 to 100)	88 (47 to 100)	97 (85 to 100)	
5/99 strain (dose 2; N=13, 8, 34)	100 (75 to 100)	100 (63 to 100)	100 (90 to 100)	
NZ 98/254 strain (dose 2; N=13, 8, 34)	15 (2 to 45)	100 (63 to 100)	94 (80 to 99)	
M10713 strain (dose 2; N=11, 8, 34)	64 (31 to 89)	75 (35 to 97)	53 (35 to 70)	

Statistical analyses

No statistical analyses for this end point

Secondary: 12) Percentage of subjects with serum bactericidal antibody titers ≥1:4 and ≥1:8 following two catch up doses of rMenB+OMV NZ vaccine given one month apart, either at 40 or 60 months of age

End point title	12) Percentage of subjects with serum bactericidal antibody titers ≥1:4 and ≥1:8 following two catch up doses of rMenB+OMV NZ vaccine given one month apart, either at 40 or 60 months of age[15]

End point description:

The percentages of subjects with hSBA ≥1:4 and ≥1:8 after two catch-up doses of rMenB+OMV NZ vaccine when given either at - 40 & 42 months or 60 & 62 months of age are reported.

Analysis was done on the MITT – Two Dose Catch Up Schedule population.

End point type	Secondary

End point timeframe:

1 month post -vaccine dose two

Notes:

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

End point values	Naive_4042	Naive_6062		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	42		
Units: Percentages of subjects				
number (confidence interval 95%)				
H44/76 strain (hSBA ≥1:4)	100 (90 to 100)	93 (81 to 99)		
H44/76 strain (hSBA ≥1:8)	100 (90 to 100)	93 (81 to 99)		
5/99 strain (hSBA ≥1:4)	100 (90 to 100)	100 (92 to 100)		
5/99 strain (hSBA ≥1:8)	100 (90 to 100)	100 (92 to 100)		
NZ 98/254 strain (hSBA ≥1:4)	94 (81 to 99)	100 (92 to 100)		
NZ 98/254 strain (hSBA ≥1:8)	94 (81 to 99)	90 (77 to 97)		
M10713 strain (hSBA ≥1:4)	89 (74 to 97)	100 (91 to 100)		
M10713 strain (hSBA ≥1:8)	86 (71 to 95)	98 (87 to 100)		

Statistical analyses

No statistical analyses for this end point

Secondary: 13) Geometric mean antibody titers in children after two catch up doses of rMenB+OMV NZ vaccine given, either at 40 or 60 months of age.

End point title	13) Geometric mean antibody titers in children after two catch up doses of rMenB+OMV NZ vaccine given, either at 40 or 60 months of age.[16]

End point description:

The geometric mean antibody titers in children after two catch-up doses of rMenB+OMV NZ vaccine when given either at - 40 & 42 months or 60 & 62 months of age are reported.

Analysis was done on the MITT – Two Dose Catch Up Schedule population.

End point type	Secondary

End point timeframe:

1 month post vaccine dose two

Notes:

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

End point values	Naive_4042	Naive_6062		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	42		
Units: Titers				
geometric mean (confidence interval 95%)				
H44/76 strain	88 (63 to 123)	34 (25 to 47)		
5/99 strain	1019 (688 to 1510)	865 (601 to 1244)		
NZ 98/254 strain	47 (32 to 69)	29 (20 to 41)		

M10713 strain (N=36, 41)	33 (24 to 47)	43 (31 to 59)		

Statistical analyses

No statistical analyses for this end point

Secondary: 14) Percentage of subjects with a 4-fold increase in antibody titers after receiving two catch up doses of rMenB+OMV NZ vaccine, either at 40 or 60 months of age

End point title	14) Percentage of subjects with a 4-fold increase in antibody titers after receiving two catch up doses of rMenB+OMV NZ vaccine, either at 40 or 60 months of age[17]

End point description:

The percentages of subjects with four-fold increase in hSBA titers over baseline against N.meningitidis B one month after receiving a two catch-up doses of rMenB+OMV NZ vaccine either at 40 & 42 months or 60 & 62 months of age are reported.

Analysis was done on the MITT – Two Dose Catch Up Schedule population.

End point type	Secondary

End point timeframe:

1 month post vaccine dose 2

Notes:

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

End point values	Naive_4042	Naive_6062		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	34	38		
Units: Percentage of subjects				
number (confidence interval 95%)				
H44/76 strain (% 4 fold increase)	97 (85 to 100)	71 (54 to 85)		
5/99 strain (% 4 fold increase)	100 (90 to 100)	100 (91 to 100)		
NZ 98/254 strain (% 4 fold increase)	94 (80 to 99)	89 (75 to 97)		
M10713 strain (% 4 fold increase)	53 (35 to 70)	21 (10 to 37)		

Statistical analyses

No statistical analyses for this end point

Secondary: 15) Persisting geometric mean antibody titers against N.meningitidis B in children at 60 months of age

End point title	15) Persisting geometric mean antibody titers against N.meningitidis B in children at 60 months of age

End point description:

The persisting GMTs against N.meningitidis B strains in children at 60 months of age who had received

one or two booster doses of either rMenB or rMenB+ OMV NZ vaccine or had received two catch-up doses of rMenB+ OMV NZ vaccine at 40 months of age in the present study are compared with GMTs in vaccine-naïve subjects.

Analysis was done on the MITT – 60 Months of Age Antibody Persistence population.

End point type	Secondary

End point timeframe:

18-20 months after last Men B vaccine; baseline for naïve_6062

End point values	5rMenB	5rMenB+OMV NZ	3rMenB	3rMenB+OMV NZ
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	24	16	13	5
Units: Titers				
geometric mean (confidence interval 95%)				
H44/76 strain (N=24, 16, 13, 5, 28, 46)	3.13 (1.75 to 5.59)	4.68 (2.3 to 9.52)	18 (8.08 to 39)	13 (3.52 to 45)
5/99 strain (N=23, 16, 13, 5, 28, 46)	43 (19 to 99)	136 (51 to 365)	369 (123 to 1103)	210 (36 to 1227)
NZ 98/254 strain	1.05 (0.8 to 1.38)	4.95 (3.54 to 6.92)	1 (0.69 to 1.45)	11 (5.93 to 20)
M10713 strain (N=22, 16, 12, 5, 27, 46)	12 (7.22 to 20)	10 (5.67 to 19)	12 (5.85 to 24)	25 (8.47 to 74)

End point values	Naive_4042	Naive_6062		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	46		
Units: Titers				
geometric mean (confidence interval 95%)				
H44/76 strain (N=24, 16, 13, 5, 28, 46)	12 (6.27 to 23)	2.98 (1.86 to 4.78)		
5/99 strain (N=23, 16, 13, 5, 28, 46)	44 (29 to 67)	1.14 (0.88 to 1.47)		
NZ 98/254 strain	2.42 (1.59 to 3.66)	1.04 (0.96 to 1.14)		
M10713 strain (N=22, 16, 12, 5, 27, 46)	8.52 (5.09 to 14)	18 (12 to 28)		

Statistical analyses

No statistical analyses for this end point

Secondary: 16) Percentage of subjects with persisting hSBA antibody titers ≥1:4 and ≥1:8 in children at 60 months of age

End point title	16) Percentage of subjects with persisting hSBA antibody titers ≥1:4 and ≥1:8 in children at 60 months of age

End point description:

The percentage of subjects with persisting hSBA titers ≥1:4 and ≥1:8 at 60 months of age against N.meningitidis B strains after having received one or two booster doses of either rMenB or rMenB+ OMV NZ vaccine or had received two catch-up doses of rMenB+ OMV NZ vaccine at 40 months of age in the present study are reported.

Analysis was done on the MITT – 60 Months of Age Antibody Persistence population.

End point type	Secondary

End point timeframe:

18-20 months after last Men B vaccine; baseline for naïve_6062

End point values	5rMenB	5rMenB+OMV NZ	3rMenB	3rMenB+OMV NZ
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	24	16	13	5
Units: Percentages of subjects				
number (confidence interval 95%)				
hSBA ≥1:4 (H44/76 strain; N=24, 16, 13, 5, 28, 46)	46 (26 to 67)	44 (20 to 70)	85 (55 to 98)	80 (28 to 99)
hSBA ≥1:4 (5/99 strain; N=23, 16, 13, 5, 28, 46)	83 (61 to 95)	88 (62 to 98)	100 (75 to 100)	100 (48 to 100)
hSBA ≥1:4 (NZ 98/254 strain)	0 (0 to 14)	69 (41 to 89)	0 (0 to 25)	80 (28 to 99)
hSBA ≥1:4 (M10713 strain; N=22, 16, 12, 5, 27, 46)	77 (55 to 92)	88 (62 to 98)	92 (62 to 100)	100 (48 to 100)
hSBA ≥1:8 (H44/76 strain; N=24, 16, 13, 5, 28, 46)	25 (10 to 47)	31 (11 to 59)	77 (46 to 95)	60 (15 to 95)
hSBA ≥1:8 (5/99 strain; N=23, 16, 13, 5, 28, 46)	74 (52 to 90)	88 (62 to 98)	100 (75 to 100)	100 (48 to 100)
hSBA ≥1:8 (NZ 98/254 strain)	0 (0 to 14)	31 (11 to 59)	0 (0 to 25)	40 (5 to 85)
hSBA ≥1:8 (M10713 strain; N=22, 16, 12, 5, 27, 46)	59 (36 to 79)	63 (35 to 85)	67 (35 to 90)	80 (28 to 99)

End point values	Naive_4042	Naive_6062		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	46		
Units: Percentages of subjects				
number (confidence interval 95%)				
hSBA ≥1:4 (H44/76 strain; N=24, 16, 13, 5, 28, 46)	71 (51 to 87)	33 (20 to 48)		
hSBA ≥1:4 (5/99 strain; N=23, 16, 13, 5, 28, 46)	100 (88 to 100)	2 (0.055 to 12)		
hSBA ≥1:4 (NZ 98/254 strain)	31 (15 to 51)	2 (0.055 to 12)		
hSBA ≥1:4 (M10713 strain; N=22, 16, 12, 5, 27, 46)	81 (62 to 94)	83 (69 to 92)		
hSBA ≥1:8 (H44/76 strain; N=24, 16, 13, 5, 28, 46)	61 (41 to 78)	26 (14 to 41)		
hSBA ≥1:8 (5/99 strain; N=23, 16, 13, 5, 28, 46)	93 (76 to 99)	2 (0.055 to 12)		
hSBA ≥1:8 (NZ 98/254 strain)	21 (8 to 40)	0 (0 to 8)		
hSBA ≥1:8 (M10713 strain; N=22, 16, 12, 5, 27, 46)	48 (29 to 68)	70 (54 to 82)		

Statistical analyses

No statistical analyses for this end point

Secondary: 17) Persisting geometric mean antibody concentrations against vaccine antigen 287-953 in children (who had previously received 4 doses of MenB vaccine in parent study) at 40 months of age

End point title	17) Persisting geometric mean antibody concentrations against vaccine antigen 287-953 in children (who had previously received 4 doses of MenB vaccine in parent study) at 40 months of age[18]

End point description:

The persisting geometric mean antibody concentrations (GMCs) against vaccine antigen 287-953 in in children (at 40 months of age) who had previously received 4 doses of either rMenB or rMen+OMV NZ vaccines in parent study , are compared with the the GMCs in vaccine-naïve children.
GMCs against vaccine antigen 287-953 were measure using enzyme linked immunosorbent assay (ELISA).

Analysis was done on the MITT – 40 Months of Age Antibody Persistence population.

End point type	Secondary

End point timeframe:

28 months after last Men B vaccination; Bbseline for Naïve_4042 group

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

End point values	5rMenB	5rMenB+OMV NZ	Naive_4042	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	28	17	40	
Units: AU/mL				
geometric mean (confidence interval 95%)	82 (59 to 113)	62 (41 to 94)	23 (19 to 26)	

Statistical analyses

No statistical analyses for this end point

Secondary: 18) Persisting geometric mean antibody concentrations against vaccine antigen 287-953 in children (who had previously received 1dose of MenB vaccine in parent study) at 40 months of age

End point title	18) Persisting geometric mean antibody concentrations against vaccine antigen 287-953 in children (who had previously received 1dose of MenB vaccine in parent study) at 40 months of age[19]

End point description:

The persisting geometric mean antibody concentrations (GMCs) against vaccine antigen 287-953 in in children (at 40 months of age) who had previously received 1 doses of either rMenB or rMen+OMV NZ vaccines in parent study , are compared with the the GMCs in vaccine-naïve children.
GMCs against vaccine antigen 287-953 were measure using enzyme linked immunosorbent assay (ELISA).

Analysis was done on the MITT – 40 Months of Age Antibody Persistence population.

End point type	Secondary

End point timeframe:

28 months after last Men B vaccination; baseline for Naïve_4042 group

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

End point values	3rMenB	3rMenB+OMV NZ	Naive_4042	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	14	8	38	
Units: AU/mL				
geometric mean (confidence interval 95%)	32 (21 to 49)	28 (16 to 50)	23 (19 to 26)	

Statistical analyses

No statistical analyses for this end point

Secondary: 19) Geometric Mean Antibody Concentrations against vaccine antigen 287-953 in Children (Who Had Previously Received 4doses of MenB Vaccine) After Receiving One Booster Dose of Either rMenB or rMenB+OMV NZ at 40 Months of Age

End point title	19) Geometric Mean Antibody Concentrations against vaccine antigen 287-953 in Children (Who Had Previously Received 4doses of MenB Vaccine) After Receiving One Booster Dose of Either rMenB or rMenB+OMV NZ at 40 Months of Age[20]

End point description:

The GMCs against vaccine antigen 287-953 in children (who had previously received four doses MenB vaccine in parent study) after a single booster dose of either rMenB or rMenB+OMV NZ vaccine given at 40 months of age, are compared with the GMCs following one catch-up dose rMenB+OMV NZ vaccine given at 40 months to vaccine-naive subjects.

Analysis was done on the MITT – Booster Response population.

End point type	Secondary

End point timeframe:

1 month post booster ; 1month post dose for naïve_4042 group

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

End point values	5rMenB	5rMenB+OMV NZ	Naive_4042	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	28	19	38	
Units: AU/mL				
geometric mean (confidence interval 95%)	5592 (3900 to 8017)	3934 (2540 to 6093)	64 (44 to 94)	

Statistical analyses

No statistical analyses for this end point

Secondary: 20) Geometric Mean Antibody concentrations against vaccine antigen 287-953 in Children After Receiving Two Booster Doses of Either rMenB or rMenB+OMV NZ at 40 &42 Months of Age

End point title	20) Geometric Mean Antibody concentrations against vaccine antigen 287-953 in Children After Receiving Two Booster Doses of Either rMenB or rMenB+OMV NZ at 40 &42 Months of Age[21]

End point description:

The GMCs against vaccine antigen 287-953 in in children (who had previously received 1 dose of either rMenB or rMen+OMV NZ vaccines in parent study) , are compared with the GMCs in children who received to catch-up doses of rMenB+OMV NZ at 40 & 42 months .

Analysis was done on the MITT - Booster Response population.

End point type	Secondary

End point timeframe:

1 month after each booster/ vaccine dose

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

End point values	3rMenB	3rMenB+OMV NZ	Naive_4042	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	8	38	
Units: AU/mL				
geometric mean (confidence interval 95%)				
after 1st booster/vaccine dose (N=13, N=7, N=38)	2100 (1100 to 4007)	1764 (731 to 4256)	64 (44 to 94)	
after 2nd booster/vaccine dose (N=13, N=8, N=36	3790 (2265 to 6342)	3660 (1899 to 7055)	3464 (2782 to 4313)	

Statistical analyses

No statistical analyses for this end point

Secondary: 21) Geometric Mean Concentrations against vaccine antigen 287-953 in Children After Two Catch up Doses of rMenB+OMV NZ Vaccine Given Either at 40 or 60 Months of Age

End point title	21) Geometric Mean Concentrations against vaccine antigen 287-953 in Children After Two Catch up Doses of rMenB+OMV NZ Vaccine Given Either at 40 or 60 Months of Age[22]

End point description:

The GMCs against vaccine antigen 287-953 in children after two catch-up doses of rMenB+OMV NZ vaccine when given either at - 40 & 42 months or 60 & 62 months of age are reported.

Analysis was done on the MITT - Booster Response population.

End point type	Secondary

End point timeframe:

1 month post vaccine dose two

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

End point values	Naive_4042	Naive_6062		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	42		
Units: AU/mL				
geometric mean (confidence interval 95%)	3464 (2672 to 4489)	1744 (1372 to 2218)		

Statistical analyses

No statistical analyses for this end point

Secondary: 22) Persisting geometric mean concentrations against vaccine antigen 287-953 in children at 60 months of age

End point title	22) Persisting geometric mean concentrations against vaccine antigen 287-953 in children at 60 months of age

End point description:

The persisting GMCs against vaccine antigen 287-953 in children at 60 months of age who had either received one or two booster doses of either rMenB or rMenB+ OMV NZ vaccine or had received two catch-up doses of rMenB+ OMV NZ vaccine at 40 months of age in the present are compared with GMCs in vaccine-naïve subjects.

Analysis was done on the MITT – 60 Months of Age Antibody Persistence population.

End point type	Secondary

End point timeframe:

18-20 months after last Men B vaccine; baseline for naïve_6062

End point values	5rMenB	5rMenB+OMV NZ	3rMenB	3rMenB+OMV NZ
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	24	16	13	5
Units: AU/mL				
geometric mean (confidence interval 95%)	670 (475 to 945)	320 (210 to 487)	280 (175 to 447)	250 (118 to 532)

End point values	Naive_4042	Naive_6062		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	47		
Units: AU/mL				
geometric mean (confidence interval 95%)	121 (88 to 166)	25 (20 to 32)		

Statistical analyses

No statistical analyses for this end point

Secondary: 23) Number of subjects reporting solicited local and systemic adverse events after a receiving two catch-up doses of rMenB+OMV NZ vaccine either at 40 months or 60 months of age

End point title	23) Number of subjects reporting solicited local and systemic adverse events after a receiving two catch-up doses of rMenB+OMV NZ vaccine either at 40 months or 60 months of age[23]

End point description:

The safety and tolerability of two catch-up doses of rMenB+OMV NZ vaccine when administered either at 40 &42 months or 60 & 62 months of age in children is assessed in terms of number of subjects with solicited local and systemic reactions following vaccination.

Analysis was done on the MITT – Two Dose Catch Up Schedule population.

End point type	Secondary

End point timeframe:

Day 1-7 after any 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: There was no statistical null hypothesis associated with this safety objective.

End point values	Naive_4042	Naive_6062		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	50		
Units: Number of subjects				
Local	42	49		
Injection-site pain	41	46		
Injection-site erythema	42	48		
Injection-site induration	23	29		
Injection-site swelling	31	27		
Systemic	38	42		
Changes in eating habits	21	23		
Sleepiness	25	23		
Vomiting	1	8		
Diarrhea	7	7		
Irritability	35	31		

Headache	8	8		
Arthralgia	16	16		
Rash	2	4		
Fever (≥38°C)	7	6		
Other	31	33		
Antipyretic preventive medication used	30	33		
Antipyretic treatment medication used	7	7		
Medically attended fever	0	1		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 1-7 after each vaccination for Solicited Adverse; Unsolicited AEs were collected throughout the study period.

Adverse event reporting additional description:

The analyses for the data in this section are from the safety set.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17

Reporting groups

Reporting group title	5rMenB

Reporting group description:

Subjects who had received four doses of rMenB vaccine (at 2,4,6 and 12 months of age) in the parent study were administered a fifth dose of rMenB vaccine, at 40 months of age in the present study.

Reporting group title	5rMenB+OMV NZ

Reporting group description:

Subjects who had received four doses of rMenB +OMV NZ vaccine (at 2,4,6 and 12 months of age) in the parent study were administered a fifth dose of rMenB +OMV NZ vaccine, at 40 months of age in the present study.

Reporting group title	3rMenB

Reporting group description:

Subjects who had previously received one dose of rMenB vaccine (at 12 months of age) were administered two doses of rMenB vaccine, at 40 and 42 months of age in the present study.

Reporting group title	3rMenB+OMV NZ

Reporting group description:

Subjects who had previously received one dose of rMenB +OMV NZ vaccine (at 12 months of age) were administered two doses of rMenB +OMV NZ vaccine, at 40 and 42 months of age in the present study.

Reporting group title	Naive_4042

Reporting group description:

Vaccine-naive subjects who received two catch -up doses of rMenB+OMV NZ vaccine at 40 and 42 months of age in the present study.

Reporting group title	Naive_6062

Reporting group description:

Vaccine-naive subjects who received two catch -up doses of rMenB+OMV NZ vaccine at 60 and 62 months of age in the present study.

Serious adverse events	5rMenB	5rMenB+OMV NZ	3rMenB
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 29 (3.45%)	1 / 19 (5.26%)	0 / 14 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
haemangioma			

subjects affected / exposed	1 / 29 (3.45%)	0 / 19 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
cystic lymphangioma			
subjects affected / exposed	0 / 29 (0.00%)	0 / 19 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
migraine			
subjects affected / exposed	0 / 29 (0.00%)	0 / 19 (0.00%)	0 / 14 (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
Blood and lymphatic system disorders			
limphadenitis			
subjects affected / exposed	0 / 29 (0.00%)	0 / 19 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
abdominal pain			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 29 (0.00%)	0 / 19 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
asthma			
subjects affected / exposed	0 / 29 (0.00%)	0 / 19 (0.00%)	0 / 14 (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			
bronchopneumonia			
subjects affected / exposed	0 / 29 (0.00%)	1 / 19 (5.26%)	0 / 14 (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

oral herpes			
subjects affected / exposed	0 / 29 (0.00%)	0 / 19 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
urinary tract infection			
subjects affected / exposed	0 / 29 (0.00%)	0 / 19 (0.00%)	0 / 14 (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	3rMenB+OMV NZ	Naive_4042	Naive_6062
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 8 (12.50%)	2 / 42 (4.76%)	2 / 50 (4.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
haemangioma			
subjects affected / exposed	0 / 8 (0.00%)	0 / 42 (0.00%)	0 / 50 (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
Congenital, familial and genetic disorders			
cystic lymphangioma			
subjects affected / exposed	1 / 8 (12.50%)	0 / 42 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
migraine			
subjects affected / exposed	0 / 8 (0.00%)	1 / 42 (2.38%)	0 / 50 (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
Blood and lymphatic system disorders			
limphadenitis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 42 (2.38%)	0 / 50 (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			

abdominal pain			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 8 (0.00%)	1 / 42 (2.38%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
asthma			
subjects affected / exposed	1 / 8 (12.50%)	0 / 42 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
bronchopneumonia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 42 (0.00%)	0 / 50 (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 / 8 (0.00%)	0 / 42 (0.00%)	1 / 50 (2.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
urinary tract infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 42 (0.00%)	1 / 50 (2.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
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	5rMenB	5rMenB+OMV NZ	3rMenB
Total subjects affected by non-serious adverse events			
subjects affected / exposed	29 / 29 (100.00%)	19 / 19 (100.00%)	14 / 14 (100.00%)
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 29 (0.00%)	1 / 19 (5.26%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Heat stroke			

subjects affected / exposed	0 / 29 (0.00%)	0 / 19 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Overdose			
subjects affected / exposed	0 / 29 (0.00%)	0 / 19 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 29 (3.45%)	0 / 19 (0.00%)	2 / 14 (14.29%)
occurrences (all)	1	0	2
Lethargy			
subjects affected / exposed	0 / 29 (0.00%)	0 / 19 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Somnolence			
subjects affected / exposed	13 / 29 (44.83%)	12 / 19 (63.16%)	8 / 14 (57.14%)
occurrences (all)	13	15	11
Blood and lymphatic system disorders			
Lymphadenitis			
subjects affected / exposed	0 / 29 (0.00%)	1 / 19 (5.26%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Injection site erythema			
alternative assessment type: Systematic			
subjects affected / exposed	28 / 29 (96.55%)	19 / 19 (100.00%)	14 / 14 (100.00%)
occurrences (all)	30	21	28
Hyperpyrexia			
subjects affected / exposed	1 / 29 (3.45%)	0 / 19 (0.00%)	1 / 14 (7.14%)
occurrences (all)	1	0	1
Injection site induration			
alternative assessment type: Systematic			
subjects affected / exposed	14 / 29 (48.28%)	9 / 19 (47.37%)	8 / 14 (57.14%)
occurrences (all)	15	9	10
Injection site pain			
subjects affected / exposed	17 / 29 (58.62%)	14 / 19 (73.68%)	8 / 14 (57.14%)
occurrences (all)	18	14	10
Injection site swelling			
alternative assessment type: Systematic			

subjects affected / exposed	13 / 29 (44.83%)	5 / 19 (26.32%)	9 / 14 (64.29%)
occurrences (all)	14	5	12
Pain			
subjects affected / exposed	0 / 29 (0.00%)	0 / 19 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	1 / 29 (3.45%)	1 / 19 (5.26%)	7 / 14 (50.00%)
occurrences (all)	1	1	8
Local swelling			
subjects affected / exposed	0 / 29 (0.00%)	0 / 19 (0.00%)	0 / 14 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 29 (0.00%)	0 / 19 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 29 (3.45%)	0 / 19 (0.00%)	1 / 14 (7.14%)
occurrences (all)	1	0	2
Constipation			
subjects affected / exposed	2 / 29 (6.90%)	0 / 19 (0.00%)	0 / 14 (0.00%)
occurrences (all)	2	0	0
Diarrhoea			
subjects affected / exposed	3 / 29 (10.34%)	1 / 19 (5.26%)	3 / 14 (21.43%)
occurrences (all)	3	1	3
Faeces discoloured			
subjects affected / exposed	0 / 29 (0.00%)	0 / 19 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Vomiting			
subjects affected / exposed	1 / 29 (3.45%)	3 / 19 (15.79%)	3 / 14 (21.43%)
occurrences (all)	1	3	3
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 29 (6.90%)	0 / 19 (0.00%)	0 / 14 (0.00%)
occurrences (all)	2	0	0
Oropharyngeal pain			

subjects affected / exposed	0 / 29 (0.00%)	1 / 19 (5.26%)	0 / 14 (0.00%)
occurrences (all)	0	2	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 29 (0.00%)	0 / 19 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Eczema			
subjects affected / exposed	1 / 29 (3.45%)	0 / 19 (0.00%)	1 / 14 (7.14%)
occurrences (all)	1	0	1
Rash			
subjects affected / exposed	4 / 29 (13.79%)	0 / 19 (0.00%)	2 / 14 (14.29%)
occurrences (all)	4	0	3
Psychiatric disorders			
Irritability			
subjects affected / exposed	14 / 29 (48.28%)	10 / 19 (52.63%)	9 / 14 (64.29%)
occurrences (all)	16	12	11
Eating disorders			
subjects affected / exposed	5 / 29 (17.24%)	10 / 19 (52.63%)	5 / 14 (35.71%)
occurrences (all)	5	15	7
Musculoskeletal and connective tissue disorders			
Arthralgia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 29 (0.00%)	6 / 19 (31.58%)	4 / 14 (28.57%)
occurrences (all)	0	6	4
Infections and infestations			
Ear infection			
subjects affected / exposed	2 / 29 (6.90%)	1 / 19 (5.26%)	2 / 14 (14.29%)
occurrences (all)	3	1	2
Eczema infected			
subjects affected / exposed	0 / 29 (0.00%)	0 / 19 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Fungal skin infection			
subjects affected / exposed	0 / 29 (0.00%)	0 / 19 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Impetigo			

subjects affected / exposed	1 / 29 (3.45%)	0 / 19 (0.00%)	1 / 14 (7.14%)
occurrences (all)	2	0	1
Localised infection			
subjects affected / exposed	1 / 29 (3.45%)	0 / 19 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Lower respiratory tract infection			
subjects affected / exposed	3 / 29 (10.34%)	0 / 19 (0.00%)	0 / 14 (0.00%)
occurrences (all)	4	0	0
Nasopharingitis			
subjects affected / exposed	0 / 29 (0.00%)	1 / 19 (5.26%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Otitis media			
subjects affected / exposed	0 / 29 (0.00%)	1 / 19 (5.26%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Rhinitis			
subjects affected / exposed	0 / 29 (0.00%)	0 / 19 (0.00%)	2 / 14 (14.29%)
occurrences (all)	0	0	2
Skin infection			
subjects affected / exposed	0 / 29 (0.00%)	0 / 19 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Tonsillitis			
subjects affected / exposed	2 / 29 (6.90%)	0 / 19 (0.00%)	0 / 14 (0.00%)
occurrences (all)	2	0	0
Urinary tract infection			
subjects affected / exposed	0 / 29 (0.00%)	1 / 19 (5.26%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Varicella			
subjects affected / exposed	0 / 29 (0.00%)	1 / 19 (5.26%)	1 / 14 (7.14%)
occurrences (all)	0	1	1

Non-serious adverse events	3rMenB+OMV NZ	Naive_4042	Naive_6062
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 8 (100.00%)	42 / 42 (100.00%)	49 / 50 (98.00%)
Injury, poisoning and procedural complications			
Fall			

subjects affected / exposed	0 / 8 (0.00%)	0 / 42 (0.00%)	0 / 50 (0.00%)
occurrences (all)	0	0	0
Heat stroke			
subjects affected / exposed	1 / 8 (12.50%)	0 / 42 (0.00%)	0 / 50 (0.00%)
occurrences (all)	1	0	0
Overdose			
subjects affected / exposed	0 / 8 (0.00%)	0 / 42 (0.00%)	0 / 50 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 8 (12.50%)	8 / 42 (19.05%)	8 / 50 (16.00%)
occurrences (all)	1	9	10
Lethargy			
subjects affected / exposed	0 / 8 (0.00%)	0 / 42 (0.00%)	0 / 50 (0.00%)
occurrences (all)	0	0	0
Somnolence			
subjects affected / exposed	6 / 8 (75.00%)	25 / 42 (59.52%)	23 / 50 (46.00%)
occurrences (all)	7	37	35
Blood and lymphatic system disorders			
Lymphadenitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 42 (0.00%)	0 / 50 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Injection site erythema			
alternative assessment type: Systematic			
subjects affected / exposed	8 / 8 (100.00%)	42 / 42 (100.00%)	48 / 50 (96.00%)
occurrences (all)	16	90	97
Hyperpyrexia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 42 (0.00%)	0 / 50 (0.00%)
occurrences (all)	0	0	0
Injection site induration			
alternative assessment type: Systematic			
subjects affected / exposed	6 / 8 (75.00%)	23 / 42 (54.76%)	29 / 50 (58.00%)
occurrences (all)	11	36	45
Injection site pain			

subjects affected / exposed	8 / 8 (100.00%)	41 / 42 (97.62%)	46 / 50 (92.00%)
occurrences (all)	15	76	86
Injection site swelling			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 8 (50.00%)	31 / 42 (73.81%)	27 / 50 (54.00%)
occurrences (all)	6	47	41
Pain			
subjects affected / exposed	1 / 8 (12.50%)	0 / 42 (0.00%)	0 / 50 (0.00%)
occurrences (all)	1	0	0
Pyrexia			
subjects affected / exposed	0 / 8 (0.00%)	7 / 42 (16.67%)	6 / 50 (12.00%)
occurrences (all)	0	9	9
Local swelling			
subjects affected / exposed	1 / 8 (12.50%)	0 / 42 (0.00%)	0 / 50 (0.00%)
occurrences (all)	1	0	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 42 (0.00%)	1 / 50 (2.00%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 8 (0.00%)	0 / 42 (0.00%)	1 / 50 (2.00%)
occurrences (all)	0	0	1
Constipation			
subjects affected / exposed	0 / 8 (0.00%)	0 / 42 (0.00%)	0 / 50 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	1 / 8 (12.50%)	8 / 42 (19.05%)	7 / 50 (14.00%)
occurrences (all)	1	8	8
Faeces discoloured			
subjects affected / exposed	0 / 8 (0.00%)	0 / 42 (0.00%)	0 / 50 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 8 (0.00%)	1 / 42 (2.38%)	8 / 50 (16.00%)
occurrences (all)	0	1	9
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	0 / 8 (0.00%)	1 / 42 (2.38%)	2 / 50 (4.00%)
occurrences (all)	0	1	2
Oropharyngeal pain			
subjects affected / exposed	0 / 8 (0.00%)	1 / 42 (2.38%)	1 / 50 (2.00%)
occurrences (all)	0	1	1
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 42 (0.00%)	0 / 50 (0.00%)
occurrences (all)	0	0	0
Eczema			
subjects affected / exposed	0 / 8 (0.00%)	0 / 42 (0.00%)	1 / 50 (2.00%)
occurrences (all)	0	0	1
Rash			
subjects affected / exposed	1 / 8 (12.50%)	2 / 42 (4.76%)	4 / 50 (8.00%)
occurrences (all)	1	3	5
Psychiatric disorders			
Irritability			
subjects affected / exposed	8 / 8 (100.00%)	35 / 42 (83.33%)	31 / 50 (62.00%)
occurrences (all)	10	62	48
Eating disorders			
subjects affected / exposed	4 / 8 (50.00%)	21 / 42 (50.00%)	23 / 50 (46.00%)
occurrences (all)	4	32	37
Musculoskeletal and connective tissue disorders			
Arthralgia			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 8 (50.00%)	16 / 42 (38.10%)	16 / 50 (32.00%)
occurrences (all)	4	24	22
Infections and infestations			
Ear infection			
subjects affected / exposed	1 / 8 (12.50%)	4 / 42 (9.52%)	1 / 50 (2.00%)
occurrences (all)	1	4	1
Eczema infected			
subjects affected / exposed	0 / 8 (0.00%)	0 / 42 (0.00%)	0 / 50 (0.00%)
occurrences (all)	0	0	0
Fungal skin infection			

subjects affected / exposed	0 / 8 (0.00%)	0 / 42 (0.00%)	0 / 50 (0.00%)
occurrences (all)	0	0	0
Impetigo			
subjects affected / exposed	0 / 8 (0.00%)	1 / 42 (2.38%)	1 / 50 (2.00%)
occurrences (all)	0	1	1
Localised infection			
subjects affected / exposed	1 / 8 (12.50%)	0 / 42 (0.00%)	0 / 50 (0.00%)
occurrences (all)	1	0	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 8 (0.00%)	1 / 42 (2.38%)	1 / 50 (2.00%)
occurrences (all)	0	1	1
Nasopharingitis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 42 (2.38%)	0 / 50 (0.00%)
occurrences (all)	0	1	0
Otitis media			
subjects affected / exposed	0 / 8 (0.00%)	0 / 42 (0.00%)	0 / 50 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 8 (0.00%)	4 / 42 (9.52%)	1 / 50 (2.00%)
occurrences (all)	0	4	1
Skin infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 42 (0.00%)	0 / 50 (0.00%)
occurrences (all)	0	0	0
Tonsillitis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 42 (2.38%)	2 / 50 (4.00%)
occurrences (all)	0	1	3
Urinary tract infection			
subjects affected / exposed	0 / 8 (0.00%)	2 / 42 (4.76%)	0 / 50 (0.00%)
occurrences (all)	0	3	0
Varicella			
subjects affected / exposed	0 / 8 (0.00%)	1 / 42 (2.38%)	0 / 50 (0.00%)
occurrences (all)	0	1	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported