Clinical trial results:
A Phase IIIB, Randomized, Observer-blind, Multicenter Study to Assess the Safety and Immunogenicity of GSK's Meningococcal Group B Vaccine When Administered Concomitantly With GSK's Meningococcal MenACWY Conjugate Vaccine to Healthy Subjects of 16-18 Years of Age

Summary

EudraCT number	2016-003722-16
Trial protocol	Outside EU/EEA IT
Global end of trial date	22 July 2024

Results information

Result version number	v1
This version publication date	02 February 2025
First version publication date	02 February 2025

Trial information

Trial identification

Sponsor protocol code	205419

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04318548
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline
Sponsor organisation address	Rue de l'Institut, 89,, Rixensart, Belgium, 1330
Public contact	GSK Response Center, GlaxoSmithKline, 044 8664357343, GSKClinicalSupportHD@gsk.com
Scientific contact	GSK Response Center, GlaxoSmithKline, 044 8664357343, GSKClinicalSupportHD@gsk.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	03 October 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 November 2023
Global end of trial reached?	Yes
Global end of trial date	22 July 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

• To assess the safety and tolerability of rMenB+OMV NZ and MenACWY, when administered concomitantly or alone, in healthy subjects 16-18 years of age.
• To demonstrate the non-inferiority of the antibody response to rMenB+OMV NZ given concomitantly with MenACWY to healthy subjects 16-18 years of age compared to rMenB+OMV NZ administered alone, as measured by serum bactericidal assay using human complement (hSBA) Geometric Mean Titers (GMTs) against N. meningitidis serogroup B indicator strains M14459 (fHbp), 96217 (NadA), NZ98/254 (PorA) and M07-0241084 (NHBA), at 1 month after the second vaccination with rMenB+OMV NZ.
• To demonstrate the non-inferiority of the antibody response to MenACWY given concomitantly with rMenB+OMV NZ to healthy subjects 16-18 years of age compared to MenACWY administered alone, as measured by hSBA GMTs against each of the N. meningitidis serogroups A, C, W and Y, at 1 month after the (study) vaccination with MenACWY.

Protection of trial subjects:

Vaccine administration was preceded by a review of the subjects' medical history (including previous vaccination and occurrence of undesirable events) and a general physical examination at the first visit and symptom-directed physical examination before subsequent vaccinations. Protocol procedures, including blood sampling, were done by a qualified healthcare professional. The subjects were observed closely for at least 30 minutes following the administration of the vaccine(s)/product(s), with appropriate medical treatment readily available in case of anaphylaxis and syncope.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 August 2020
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	Italy: 111
Country: Number of subjects enrolled	United States: 834
Worldwide total number of subjects	945
EEA total number of subjects	111

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)	0
Adolescents (12-17 years)	864
Adults (18-64 years)	81
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study ended on Day 271 for participants who had not reached Day 271 when Protocol Amendment 7 took effect, and on Day 451 for those who had already passed Day 271.Safety follow-up period for each participant was from Day 1 up to Day 451 or Day 271 for participants who have not reached Day 271 at the time Protocol Amendment 7 took effect.

Pre-assignment

Screening details:

A total of 945 participants were enrolled in the study, of which only 940 were randomized into the 3 treatment groups. After randomization, 2 participants did not receive the vaccine and making it a total of 938 participants in the exposed set.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Monitor, Data analyst, Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	MenB+MenACWY Group

Arm description:

Participants received 1 dose of rMenB+OMV NZ vaccine administered concomitantly with 1 dose of MenACWY vaccine, as separate injections in each arm at Day 1, 1 dose of rMenB+OMV NZ vaccine at Day 61 and 1 dose of placebo at Day 91.

Arm type	Experimental
Investigational medicinal product name	MenACWY
Investigational medicinal product code	
Other name	Menveo
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 dose of MenACWY vaccine administered intramuscularly.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

1 dose of Placebo administered intramuscularly.

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

Dosage and administration details:

2 dose of rMenB+OMV NZ vaccine administered intramuscularly.

Arm title	MenB Group

Arm description:

Participants received 1 dose of rMenB+OMV NZ vaccine administered concomitantly with 1 dose of

placebo, as separate injections in each arm at Day 1, 1 dose of rMenB+OMV NZ vaccine at Day 61 and 1 dose of MenACWY at Day 91.

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

Dosage and administration details:

2 dose of rMenB+OMV NZ vaccine administered intramuscularly.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

1 dose of Placebo administered intramuscularly.

Investigational medicinal product name	MenACWY
Investigational medicinal product code	
Other name	Menveo
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 dose of MenACWY vaccine administered intramuscularly.

Arm title	MenACWY Group

Arm description:

Participants received 1 dose of MenACWY vaccine administered concomitantly with 1 dose of placebo, as separate injections in each arm at Day1, 1 dose of rMenB+OMV NZ vaccine each administered at Day 61 and at Day 91.

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

Dosage and administration details:

2 dose of rMenB+OMV NZ vaccine administered intramuscularly.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

1 dose of Placebo administered intramuscularly.

Investigational medicinal product name	MenACWY
Investigational medicinal product code	
Other name	Menveo
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 dose of MenACWY vaccine administered intramuscularly.

Number of subjects in period 1[1]	MenB+MenACWY Group	MenB Group	MenACWY Group
Started	310	308	320
Completed	297	284	298
Not completed	13	24	22
Adverse event, non-fatal	-	-	1
Migrated / moved from the study area	-	-	1
Not specified	1	2	3
Lost to follow-up	6	13	9
Consent withdrawal, not due to a (S)AE	5	9	6
Protocol deviation	1	-	2

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: A total of 945 participants were enrolled in the study, of which only 940 were randomized into the 3 treatment groups. After randomization, 2 participants did not receive the vaccine and making it a total of 938 participants in the exposed set.

Baseline characteristics

Reporting groups	
Reporting group title	MenB+MenACWY Group
Reporting group description:	
Participants received 1 dose of rMenB+OMV NZ vaccine administered concomitantly with 1 dose of MenACWY vaccine, as separate injections in each arm at Day 1, 1 dose of rMenB+OMV NZ vaccine at Day 61 and 1 dose of placebo at Day 91.	
Reporting group title	MenB Group
Reporting group description:	
Participants received 1 dose of rMenB+OMV NZ vaccine administered concomitantly with 1 dose of placebo, as separate injections in each arm at Day 1, 1 dose of rMenB+OMV NZ vaccine at Day 61 and 1 dose of MenACWY at Day 91.	
Reporting group title	MenACWY Group
Reporting group description:	
Participants received 1 dose of MenACWY vaccine administered concomitantly with 1 dose of placebo, as separate injections in each arm at Day1, 1 dose of rMenB+OMV NZ vaccine each administered at Day 61 and at Day 91.	

Reporting group values	MenB+MenACWY Group	MenB Group	MenACWY Group
Number of subjects	310	308	320
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	286	283	288
Adults (18-64 years)	24	25	32
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	16.4	16.4	16.5
standard deviation	± 0.7	± 0.7	± 0.7
Sex: Female, Male Units: Participants			
Male	154	170	157
Female	156	138	163
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	46	38	37
Not Hispanic or Latino	263	270	282
Unknown or Not Reported	1	0	1

Reporting group values	Total		
Number of subjects	938		

Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	857		
Adults (18-64 years)	81		
From 65-84 years	0		
85 years and over	0		
Age Continuous Units: years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male Units: Participants			
Male	481		
Female	457		
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	121		
Not Hispanic or Latino	815		
Unknown or Not Reported	2		

End points

End points reporting groups

Reporting group title	MenB+MenACWY Group
Reporting group description:	
Participants received 1 dose of rMenB+OMV NZ vaccine administered concomitantly with 1 dose of MenACWY vaccine, as separate injections in each arm at Day 1, 1 dose of rMenB+OMV NZ vaccine at Day 61 and 1 dose of placebo at Day 91.	
Reporting group title	MenB Group
Reporting group description:	
Participants received 1 dose of rMenB+OMV NZ vaccine administered concomitantly with 1 dose of placebo, as separate injections in each arm at Day 1, 1 dose of rMenB+OMV NZ vaccine at Day 61 and 1 dose of MenACWY at Day 91.	
Reporting group title	MenACWY Group
Reporting group description:	
Participants received 1 dose of MenACWY vaccine administered concomitantly with 1 dose of placebo, as separate injections in each arm at Day1, 1 dose of rMenB+OMV NZ vaccine each administered at Day 61 and at Day 91.	

Primary: Number of participants with solicited local adverse events (AEs) after the vaccination with rMenB+OMV NZ at Day 1

End point title	Number of participants with solicited local adverse events (AEs) after the vaccination with rMenB+OMV NZ at Day 1[1]
End point description:	
Solicited local adverse events assessed are injection site pain, erythema, swelling, induration. Any solicited local AEs = occurrence of the symptom regardless of intensity grade. Analysis was performed on the Exposed set (ES), which included all participants who received at least one dose of the study treatment and had the electronic diary (eDiary) for solicited events completed after the administration of study treatment and for whom data were available during the specified period. Allocation per group is based on the treatment administered. Only participants with data available at specified timepoints were included in the analysis.	
End point type	Primary
End point timeframe:	
During 7 days after the rMenB+OMV NZ vaccination at Day 1	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of this primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	MenB+MenACWY Group	MenB Group	MenACWY Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	307	306	0[2]	
Units: Participants				
Erythema	12	12		
Induration	14	22		
Pain	246	247		
Swelling	15	18		

Notes:

[2] - Participants in this group did not receive rMenB+OMV NZ on Day 1 hence zero participants.

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with solicited local adverse events (AEs) after the vaccination with rMenB+OMV NZ at Day 91

End point title	Number of participants with solicited local adverse events (AEs) after the vaccination with rMenB+OMV NZ at Day 91[3]

End point description:

Solicited local adverse events assessed are injection site pain, erythema, swelling, induration. Any solicited local AEs = occurrence of the symptom regardless of intensity grade. Analysis was performed on the Exposed set (ES), which included all participants who received at least one dose of the study treatment and had the electronic diary (eDiary) for solicited events completed after the administration of study treatment and for whom data were available during the specified period. Allocation per group is based on the treatment administered. Only participants with data available at specified timepoints were included in the analysis.

End point type	Primary

End point timeframe:

During 7 days after the rMenB+OMV NZ vaccination at Day 91

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: The analysis of this primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	MenB+MenACWY Group	MenB Group	MenACWY Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[4]	0[5]	287	
Units: Participants				
Erythema			14	
Induration			11	
Pain			205	
Swelling			13	

Notes:

[4] - Participants in this group did not receive rMenB+OMV NZ on Day 91 hence zero participants.

[5] - Participants in this group did not receive rMenB+OMV NZ on Day 91 hence zero participants.

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with solicited local adverse events (AEs) after the vaccination with rMenB+OMV NZ at Day 61

End point title	Number of participants with solicited local adverse events (AEs) after the vaccination with rMenB+OMV NZ at Day 61[6]

End point description:

Solicited local adverse events assessed are injection site pain, erythema, swelling, induration. Any solicited local AEs = occurrence of the symptom regardless of intensity grade. Analysis was performed on the Exposed set (ES), which included all participants who received at least one dose of the study treatment and had the electronic diary (eDiary) for solicited events completed after the administration of study treatment and for whom data were available during the specified period. Allocation per group is based on the treatment administered. Only participants with data available at specified timepoints were included in the analysis.

End point type	Primary

End point timeframe:

During 7 days after the rMenB+OMV NZ vaccination at Day 61

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of this primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	MenB+MenACWY Group	MenB Group	MenACWY Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	307	306	287	
Units: Participants				
Erythema	17	17	8	
Induration	18	19	6	
Pain	240	228	238	
Swelling	16	16	7	

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with solicited local AEs after the vaccination with MenACWY at Day 1

End point title	Number of participants with solicited local AEs after the vaccination with MenACWY at Day 1[7]

End point description:

Solicited local adverse events assessed are injection site pain, erythema, swelling, induration. Any solicited local AEs= occurrence of the symptom regardless of intensity grade. Analysis was performed on ES population. Only participants with data available at specified timepoints were included in the analysis.

End point type	Primary

End point timeframe:

During 7 days after the MenACWY vaccination at Day 1

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of this primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	MenB+MenACWY Group	MenB Group	MenACWY Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	307	0[8]	319	
Units: Participants				
Erythema	5		6	
Induration	7		7	
Pain	93		104	
Swelling	5		5	

Notes:

[8] - Participants in this group did not receive MenACWY on Day 1 hence zero participants.

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with solicited local AEs after the vaccination with MenACWY at Day 61

End point title	Number of participants with solicited local AEs after the vaccination with MenACWY at Day 61[9]

End point description:

Solicited local adverse events assessed are injection site pain, erythema, swelling, induration. Any solicited local AEs= occurrence of the symptom regardless of intensity grade. Analysis was performed on ES population. Only participants with data available at specified timepoints were included in the analysis. 1 participant in MenB Group received wrong study treatment at Day 61 (MenACWY vaccine instead of rMenB+OMV NZ), hence was considered in the analysis population.

End point type	Primary

End point timeframe:

During 7 days after the MenACWY vaccination at Day 61

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of this primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	MenB+MenACWY Group	MenB Group	MenACWY Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[10]	1	0[11]	
Units: Participants				
Erythema		0		
Induration		0		
Pain		1		
Swelling		0		

Notes:

[10] - Participants in this group did not receive MenACWY on Day 61 hence zero participants.

[11] - Participants in this group did not receive MenACWY on Day 61 hence zero participants.

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with solicited local AEs after the vaccination with MenACWY at Day 91

End point title	Number of participants with solicited local AEs after the vaccination with MenACWY at Day 91[12]

End point description:

Solicited local adverse events assessed are injection site pain, erythema, swelling, induration. Any solicited local AEs= occurrence of the symptom regardless of intensity grade. Analysis was performed on ES population. Only participants with data available at specified timepoints were included in the analysis.

End point type	Primary

End point timeframe:

During 7 days after the MenACWY vaccination at Day 91

Notes:

[12] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of this primary endpoint was descriptive i.e. no statistical hypothesis test was

performed.

End point values	MenB+MenACWY Group	MenB Group	MenACWY Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[13]	265	0[14]	
Units: Participants				
Erythema		4		
Induration		1		
Pain		38		
Swelling		5		

Notes:

[13] - Participants in this group did not receive MenACWY on Day 91 hence zero participants.

[14] - Participants in this group did not receive MenACWY on Day 91 hence zero participants.

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with solicited local AEs after the vaccination with Placebo at Day 1

End point title	Number of participants with solicited local AEs after the vaccination with Placebo at Day 1[15]

End point description:

Solicited local adverse events assessed are injection site pain, erythema, swelling, induration. Any solicited local AEs = occurrence of the symptom regardless of intensity grade. Analysis was performed on ES population. Only participants with data available at specified timepoints were included in the analysis.

End point type	Primary

End point timeframe:

During 7 days after the Placebo vaccination at Day 1

Notes:

[15] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of this primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	MenB+MenACWY Group	MenB Group	MenACWY Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[16]	306	320	
Units: Participants				
Erythema		2	2	
Induration		5	0	
Pain		78	77	
Swelling		2	1	

Notes:

[16] - Participants in this group did not receive Placebo on Day 1 hence zero participants.

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with solicited local AEs after the vaccination with Placebo at Day 91

End point title	Number of participants with solicited local AEs after the vaccination with Placebo at Day 91[17]

End point description:

Solicited local adverse events assessed are injection site pain, erythema, swelling, induration. Any solicited local AEs = occurrence of the symptom regardless of intensity grade. Analysis was performed on ES population. Only participants with data available at specified timepoints were included in the analysis. 1 participant in MenACWY Group received wrong study treatment at Day 91 (placebo instead of rMenB+OMV NZ), hence was considered in the analysis population.

End point type	Primary

End point timeframe:

During 7 days after the Placebo vaccination at Day 91

Notes:

[17] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of this primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	MenB+MenACWY Group	MenB Group	MenACWY Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	282	0[18]	320	
Units: Participants				
Erythema	1		0	
Induration	1		0	
Pain	25		0	
Swelling	0		0	

Notes:

[18] - Participants in this group did not receive Placebo on Day 91 hence zero participants.

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with solicited systemic AEs at Day 1

End point title	Number of participants with solicited systemic AEs at Day 1[19]

End point description:

Solicited systemic adverse events assessed are fever [temperature >= 38.0°C], nausea, fatigue, myalgia, arthralgia, and headache. Analysis was performed on ES population. Only participants with data available at specified timepoints were included in the analysis.

End point type	Primary

End point timeframe:

During 7 days after the first study intervention administration occurring at Day 1

Notes:

[19] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of this primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	MenB+MenACWY Group	MenB Group	MenACWY Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	307	306	320	
Units: Participants				
Arthralgia	24	32	24	
Fatigue	114	118	108	
Headache	128	135	134	
Myalgia	36	49	31	
Nausea	46	57	51	
Fever	7	10	2	

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with solicited systemic AEs at Day 61

End point title	Number of participants with solicited systemic AEs at Day 61[20]

End point description:

Solicited systemic adverse events assessed are fever [temperature >= 38.0°C], nausea, fatigue, myalgia, arthralgia, and headache. Analysis was performed on ES population. Only participants with data available at specified timepoints were included in the analysis.

End point type	Primary

End point timeframe:

During 7 days after the second study intervention administration occurring at Day 61

Notes:

[20] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of this primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	MenB+MenACWY Group	MenB Group	MenACWY Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	307	306	320	
Units: Participants				
Arthralgia	28	24	27	
Fatigue	96	101	88	
Headache	112	103	93	
Myalgia	41	42	43	
Nausea	37	37	40	
Fever	4	8	6	

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with solicited systemic AEs at Day 91

End point title	Number of participants with solicited systemic AEs at Day 91[21]

End point description:

Solicited systemic adverse events assessed are fever [temperature >= 38.0°C], nausea, fatigue, myalgia, arthralgia, and headache. Analysis was performed on ES population. Only participants with data available at specified timepoints were included in the analysis.

End point type	Primary

End point timeframe:

During 7 days after the third study intervention administration occurring at Day 91

Notes:

[21] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of this primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	MenB+MenACWY Group	MenB Group	MenACWY Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	307	306	320	
Units: Participants				
Arthralgia	7	8	24	
Fatigue	38	59	86	
Headache	56	53	84	
Myalgia	7	16	39	
Nausea	20	18	31	
Fever	2	2	6	

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with any unsolicited AEs (including all Serious Adverse Events) at Day 61

End point title	Number of participants with any unsolicited AEs (including all Serious Adverse Events) at Day 61[22]

End point description:

Unsolicited adverse events are defined as any AE reported in addition to those solicited during the clinical study. Also, any 'solicited' symptom with onset outside the specified period of follow-up for solicited symptoms are reported as an unsolicited adverse event. Any solicited AE that has not resolved within 30 days post vaccination and is reported during clinic visits or safety follow-up calls is entered into the subject's electronic Case Report Form (eCRF) as an unsolicited AE. Serious Adverse Events (SAEs) are any untoward medical occurrence that result in death, are life-threatening, require hospitalization or prolongation of existing hospitalization, result in disability/incapacity and is a congenital anomaly/birth defect in the offspring of a study subject. Analysis was performed on ES population. Only participants with data available at specified timepoints were included in the analysis.

End point type	Primary

End point timeframe:

During 30 days after the second study intervention administration occurring at Day 61

Notes:

[22] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of this primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	MenB+MenACWY Group	MenB Group	MenACWY Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	310	308	320	
Units: Participants	51	47	44	

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with any unsolicited AEs (including all Serious Adverse Events) at Day 1

End point title	Number of participants with any unsolicited AEs (including all Serious Adverse Events) at Day 1[23]

End point description:

Unsolicited adverse events are defined as any AE reported in addition to those solicited during the clinical study. Also, any 'solicited' symptom with onset outside the specified period of follow-up for solicited symptoms are reported as an unsolicited adverse event. Any solicited AE that has not resolved within 30 days post vaccination and is reported during clinic visits or safety follow-up calls is entered into the subject's electronic Case Report Form (eCRF) as an unsolicited AE. Serious Adverse Events (SAEs) are any untoward medical occurrence that result in death, are life-threatening, require hospitalization or prolongation of existing hospitalization, result in disability/incapacity and is a congenital anomaly/birth defect in the offspring of a study subject. Analysis was performed on ES population. Only participants with data available at specified timepoints were included in the analysis.

End point type	Primary

End point timeframe:

During 30 days after the first study intervention administration occurring at Day 1

Notes:

[23] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of this primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	MenB+MenACWY Group	MenB Group	MenACWY Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	310	308	320	
Units: Participants	49	54	55	

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with any AEs/SAEs leading to withdrawal at Day 61

End point title	Number of participants with any AEs/SAEs leading to withdrawal at Day 61[24]

End point description:

Unsolicited AEs are any AE reported beyond those solicited during the clinical study. A solicited symptom reported outside the designated follow-up period is considered an unsolicited AE. Any solicited AE that has not resolved within 30 days post vaccination and is reported during clinic visits/safety follow-up calls is entered into the subject's eCRF as an unsolicited AE. SAEs are any untoward medical occurrence that result in death, are life-threatening, require hospitalization/prolongation of existing hospitalization,

result in disability/incapacity and is a congenital anomaly/birth defect in the offspring of a study subject. A participant was considered a 'withdrawal' from study when no study procedure has occurred, no follow-up has been performed and no further information has been collected for this participant from the date of withdrawal/last contact. Analysis was performed on ES population,participants with data available at specified timepoints were included in the analysis.

End point type	Primary

End point timeframe:

During 30 days after the second study intervention administration occurring at Day 61

Notes:

[24] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of this primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	MenB+MenACWY Group	MenB Group	MenACWY Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	310	308	320	
Units: Participants	0	0	0	

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with any AEs/SAEs leading to withdrawal at Day 1

End point title	Number of participants with any AEs/SAEs leading to withdrawal at Day 1[25]

End point description:

Unsolicited AEs are any AE reported beyond those solicited during the clinical study. A solicited symptom reported outside the designated follow-up period is considered an unsolicited AE. Any solicited AE that has not resolved within 30 days post vaccination and is reported during clinic visits/safety follow-up calls is entered into the subject's eCRF as an unsolicited AE. SAEs are any untoward medical occurrence that result in death, are life-threatening, require hospitalization/prolongation of existing hospitalization, result in disability/incapacity and is a congenital anomaly/birth defect in the offspring of a study subject. A participant was considered a 'withdrawal' from study when no study procedure has occurred, no follow-up has been performed and no further information has been collected for this participant from the date of withdrawal/last contact. Analysis was performed on ES population,participants with data available at specified timepoints were included in the analysis.

End point type	Primary

End point timeframe:

During 30 days after the first study intervention administration occurring at Day 1

Notes:

[25] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of this primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	MenB+MenACWY Group	MenB Group	MenACWY Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	310	308	320	
Units: Participants	0	0	1	

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with any unsolicited AEs (including all Serious Adverse Events) at Day 91

End point title	Number of participants with any unsolicited AEs (including all Serious Adverse Events) at Day 91[26]

End point description:

Unsolicited adverse events are defined as any AE reported in addition to those solicited during the clinical study. Also, any 'solicited' symptom with onset outside the specified period of follow-up for solicited symptoms are reported as an unsolicited adverse event. Any solicited AE that has not resolved within 30 days post vaccination and is reported during clinic visits or safety follow-up calls is entered into the subject's electronic Case Report Form (eCRF) as an unsolicited AE. Serious Adverse Events (SAEs) are any untoward medical occurrence that result in death, are life-threatening, require hospitalization or prolongation of existing hospitalization, result in disability/incapacity and is a congenital anomaly/birth defect in the offspring of a study subject. Analysis was performed on ES population. Only participants with data available at specified timepoints were included in the analysis.

End point type	Primary

End point timeframe:

During 30 days after the third study intervention administration occurring at Day 91

Notes:

[26] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of this primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	MenB+MenACWY Group	MenB Group	MenACWY Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	310	308	320	
Units: Participants	37	37	38	

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with any AEs/SAEs leading to withdrawal at Day 91

End point title	Number of participants with any AEs/SAEs leading to withdrawal at Day 91[27]

End point description:

Unsolicited AEs are any AE reported beyond those solicited during the clinical study. A solicited symptom reported outside the designated follow-up period is considered an unsolicited AE. Any solicited AE that has not resolved within 30 days post vaccination and is reported during clinic visits/safety follow-up calls is entered into the subject's eCRF as an unsolicited AE. SAEs are any untoward medical occurrence that result in death, are life-threatening, require hospitalization/prolongation of existing hospitalization, result in disability/incapacity and is a congenital anomaly/birth defect in the offspring of a study subject. A participant was considered a 'withdrawal' from study when no study procedure has occurred, no follow-up has been performed and no further information has been collected for this participant from the

date of withdrawal/last contact. Analysis was performed on ES population,participants with data available at specified timepoints were included in the analysis.

End point type	Primary

End point timeframe:

During 30 days after the third study intervention administration occurring at Day 91

Notes:

[27] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of this primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	MenB+MenACWY Group	MenB Group	MenACWY Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	310	308	320	
Units: Participants	0	0	0	

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with any medically attended AEs at Day 61

End point title	Number of participants with any medically attended AEs at Day 61[28]

End point description:

Medically attended AEs are symptoms or illnesses requiring hospitalization, or emergency room visit, or visit to/by a health care provider. Analysis was performed on ES population. Only participants with data available at specified timepoints were included in the analysis.

End point type	Primary

End point timeframe:

During 30 days after the second study intervention administration occurring at Day 61

Notes:

[28] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of this primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	MenB+MenACWY Group	MenB Group	MenACWY Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	310	308	320	
Units: Participants	28	32	25	

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with any medically attended AEs at Day 1

End point title	Number of participants with any medically attended AEs at Day

	1[29]

End point description:

Medically attended AEs are symptoms or illnesses requiring hospitalization, or emergency room visit, or visit to/by a health care provider. Analysis was performed on ES population. Only participants with data available at specified timepoints were included in the analysis.

End point type	Primary

End point timeframe:

During 30 days after the first study intervention administration occurring at Day 1

Notes:

[29] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of this primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	MenB+MenACWY Group	MenB Group	MenACWY Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	310	308	320	
Units: Participants	28	36	26	

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants who received rMenB+OMV NZ with adverse events of special interest (AESI)

End point title	Number of participants who received rMenB+OMV NZ with adverse events of special interest (AESI)[30]

End point description:

AESIs are predefined (serious or non-serious) adverse events of scientific and medical concern specific to the product or program, for which ongoing monitoring and rapid communication by the investigator to the sponsor can be appropriate, because such an event might warrant further investigation in order to characterize and understand it. Analysis was performed on ES population. Only participants with data available at specified timepoints were included in the analysis.

End point type	Primary

End point timeframe:

Throughout the study period (Day 1 to Day 271)

Notes:

[30] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of this primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	MenB+MenACWY Group	MenB Group	MenACWY Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	310	308	320	
Units: Participants	0	0	0	

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with any SAEs, AEs leading to withdrawal and medically attended AEs

End point title	Number of participants with any SAEs, AEs leading to withdrawal and medically attended AEs[31]

End point description:

SAEs, AEs leading to withdrawal and medically attended AEs were assessed throughout the study period and are reported in this outcome measure. Analysis was performed on the ES population, which included all participants who received at least one dose of the study treatment. Allocation per group is based on the treatment administered.

End point type	Primary

End point timeframe:

Throughout the study period (Day 1 to Day 271)

Notes:

[31] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of this primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	MenB+MenACWY Group	MenB Group	MenACWY Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	310	308	320	
Units: Participants				
SAEs	2	3	5	
AEs leading to withdrawal	0	0	1	
Medically attended AEs	93	103	96	

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with any medically attended AEs at Day 91

End point title	Number of participants with any medically attended AEs at Day 91[32]

End point description:

Medically attended AEs are symptoms or illnesses requiring hospitalization, or emergency room visit, or visit to/by a health care provider. Analysis was performed on ES population. Only participants with data available at specified timepoints were included in the analysis.

End point type	Primary

End point timeframe:

During 30 days after the third study intervention administration occurring at Day 91

Notes:

[32] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of this primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	MenB+MenACWY Group	MenB Group	MenACWY Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	310	308	320	
Units: Participants	19	21	17	

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with any SAEs and AEs leading to withdrawal

End point title	Number of participants with any SAEs and AEs leading to withdrawal[33]

End point description:

Unsolicited AEs are any AE reported beyond those solicited during the clinical study. A solicited symptom reported outside the designated follow-up period is considered an unsolicited AE. Any solicited AE that has not resolved within 30 days post vaccination and is reported during clinic visits/safety follow-up calls is entered into the subject's eCRF as an unsolicited AE. SAEs are any untoward medical occurrence that result in death, are life-threatening, require hospitalization or prolongation, causing disability/incapacity and is a congenital anomaly/birth defect in the offspring of study subject. A participant is considered a 'withdrawal' from the study if no further study procedures, follow-ups, or data collection have occurred since the withdrawal/last contact date. Analysis was performed on ES population,participants with data available at specified timepoints (during safety follow-up period from Day 271 to Day 451) were included in the analysis.

End point type	Primary

End point timeframe:

During safety follow-up (Day 271 to Day 451)

Notes:

[33] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of this primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	MenB+MenACWY Group	MenB Group	MenACWY Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	88	90	87	
Units: Participants				
SAEs	0	1	2	
AEs leading to withdrawal	0	0	0	

Statistical analyses

No statistical analyses for this end point

Primary: Human Serum Bactericidal Assay (hSBA) Geometric Mean Titers (GMTs) against each of the N. meningitidis serogroup B strains at 1 month after the second vaccination with rMenB+OMV NZ (groups MenB+MenACWY and MenB), and between-group GMT ratios

End point title	Human Serum Bactericidal Assay (hSBA) Geometric Mean Titers (GMTs) against each of the N. meningitidis serogroup B

	strains at 1 month after the second vaccination with rMenB+OMV NZ (groups MenB+MenACWY and MenB), and between-group GMT ratios[34]

End point description:

hSBA titers were measured by serum bactericidal assay and expressed as Geometric Mean Titers (GMTs) against N. meningitidis serogroup B indicator strains (M14459 [fHbp], 96217 [NadA], NZ98/254 [PorA] and M13520 [NHBA]). Analysis was performed on the Per Protocol Set (PPS), which included participants who received at least 1 dose of the study intervention to which they were randomized and had post-vaccination data available at the specified timepoint minus participants with protocol deviations that led to exclusion from the PPS.

End point type	Primary

End point timeframe:

At Day 91 (1 month after the second vaccination with rMenB+OMV NZ in MenB+MenACWY and MenB groups)

Notes:

[34] - 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: As specified in the Protocol, the analysis assess the imqmune response to rMenB+OMV NZ in healthy subjects 16-18 years of age against N. meningitidis serogroup B test strains M14459 (fHbp), 96217 (NadA), NZ98/254 (PorA) and M07-0241084 (NHBA), at one month after the second vaccination with rMenB+OMV NZ.

End point values	MenB+MenACWY Group	MenB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	274	267		
Units: Titers				
geometric mean (confidence interval 95%)				
fHbp (M14459)	16.9 (14.4 to 19.8)	18.7 (15.9 to 21.9)		
NadA (96217)	239.6 (202.9 to 283.0)	272.4 (231.1 to 321.0)		
PorA (NZ98/254)	18.8 (15.6 to 22.6)	21.3 (17.7 to 25.6)		
NHBA (M13520)	19.0 (15.6 to 23.1)	20.5 (16.9 to 24.9)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

To demonstrate the non-inferiority (NI) of the antibody response to rMenB+OMV NZ given concomitantly with MenACWY compared to rMenB+OMV NZ administered alone, measured by hSBA GMTs against N. meningitidis serogroup B indicator strains at one month after the second vaccination with rMenB+OMV NZ (at Day 91).

Comparison groups	MenB+MenACWY Group v MenB Group
Number of subjects included in analysis	541
Analysis specification	Pre-specified
Analysis type	
Method	ANOVA
Parameter estimate	GMT Ratio
Point estimate	0.9

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.77
upper limit	1.06

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

To demonstrate the non-inferiority of the antibody response to rMenB+OMV NZ given concomitantly with MenACWY compared to rMenB+OMV NZ administered alone, measured by hSBA GMTs against N. meningitidis serogroup B indicator strains at one month after the second vaccination with rMenB+OMV NZ (at Day 91).

Comparison groups	MenB+MenACWY Group v MenB Group
Number of subjects included in analysis	541
Analysis specification	Pre-specified
Analysis type	
Method	ANOVA
Parameter estimate	GMT Ratio
Point estimate	0.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.75
upper limit	1.04

Statistical analysis title	Statistical Analysis 3

Statistical analysis description:

To demonstrate the non-inferiority of the antibody response to rMenB+OMV NZ given concomitantly with MenACWY compared to rMenB+OMV NZ administered alone, measured by hSBA GMTs against N. meningitidis serogroup B indicator strains at one month after the second vaccination with rMenB+OMV NZ (at Day 91).

Comparison groups	MenB+MenACWY Group v MenB Group
Number of subjects included in analysis	541
Analysis specification	Pre-specified
Analysis type	
Method	ANOVA
Parameter estimate	GMT Ratio
Point estimate	0.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.76
upper limit	1.12

Statistical analysis title	Statistical Analysis 4

Statistical analysis description:

To demonstrate the non-inferiority of the antibody response to rMenB+OMV NZ given concomitantly with MenACWY compared to rMenB+OMV NZ administered alone, measured by hSBA GMTs against N. meningitidis serogroup B indicator strains at one month after the second vaccination with rMenB+OMV NZ (at Day 91).

Comparison groups	MenB+MenACWY Group v MenB Group
Number of subjects included in analysis	541
Analysis specification	Pre-specified
Analysis type	
Method	ANOVA
Parameter estimate	GMT Ratio
Point estimate	0.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.73
upper limit	1.06

Primary: Number of participants who received rMenB+OMV NZ with AESI

End point title	Number of participants who received rMenB+OMV NZ with AESI[35]

End point description:

AESIs are predefined (serious or non-serious) adverse events of scientific and medical concern specific to the product or program, for which ongoing monitoring and rapid communication by the investigator to the sponsor can be appropriate, because such an event might warrant further investigation in order to characterize and understand it. Analysis was performed on ES population. Only participants with data available at specified timepoints (during safety follow-up period from Day 271 to Day 451) were included in the analysis.

End point type	Primary

End point timeframe:

During safety follow-up (Day 271 to Day 451)

Notes:

[35] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of this primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	MenB+MenACWY Group	MenB Group	MenACWY Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	88	90	87	
Units: Participants	0	0	0	

Statistical analyses

No statistical analyses for this end point

Primary: hSBA GMTs against each of the N. meningitidis serogroups A, C, W and Y after vaccination with MenACWY (groups MenB+MenACWY and MenACWY), and between-group GMT ratios

End point title	hSBA GMTs against each of the N. meningitidis serogroups A, C, W and Y after vaccination with MenACWY (groups MenB+MenACWY and MenACWY), and between-group GMT ratios[36]

End point description:

hSBA titers were measured by serum bactericidal assay and expressed as GMTs against each of the 4 serogroups Men A, Men C, Men W and Men Y. Analysis was performed on PPS population. Only those participants with data available at specified timepoint were included in analysis.

End point type	Primary

End point timeframe:

At Day 31 (1 month after the vaccination with MenACWY in MenACWY and MenB+MenACWY groups)

Notes:

[36] - 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: As specified in the Protocol, the analysis assess the immune response to MenACWY in healthy subjects 16-18 years of age against each of the serogroups A, C, W and Y, at one month after the (study) vaccination with MenACWY.

End point values	MenB+MenACWY Group	MenACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	295	303		
Units: Titers				
geometric mean (confidence interval 95%)				
Men A	2388.8 (1977.2 to 2886.1)	2536.1 (2095.7 to 3069.1)		
Men C	2075.9 (1602.5 to 2689.3)	1867.6 (1438.7 to 2424.2)		
Men W	2299.3 (1902.5 to 2778.9)	2305.7 (1905.3 to 2790.4)		
Men Y	2897.3 (2359.2 to 3558.3)	2802.0 (2278.3 to 3446.2)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

To demonstrate the non-inferiority of the antibody response to MenACWY given concomitantly with rMenB+OMV NZ compared to MenACWY administered alone, as measured by hSBA GMTs against the N. meningitidis serogroup Men A, at one month after the vaccination with MenACWY (at Day 31).

Comparison groups	MenB+MenACWY Group v MenACWY Group
Number of subjects included in analysis	598
Analysis specification	Pre-specified
Analysis type	
Method	ANOVA
Parameter estimate	GMT Ratio
Point estimate	0.94

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.78
upper limit	1.14

Statistical analysis title	Statistical Analysis 4

Statistical analysis description:

To demonstrate the non-inferiority of the antibody response to MenACWY given concomitantly with rMenB+OMV NZ compared to MenACWY administered alone, as measured by hSBA GMTs against the N. meningitidis serogroup Men Y, at one month after the vaccination with MenACWY (at Day 31).

Comparison groups	MenB+MenACWY Group v MenACWY Group
Number of subjects included in analysis	598
Analysis specification	Pre-specified
Analysis type	
Method	ANOVA
Parameter estimate	GMT Ratio
Point estimate	1.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.84
upper limit	1.27

Statistical analysis title	Statistical Analysis 3

Statistical analysis description:

To demonstrate the non-inferiority of the antibody response to MenACWY given concomitantly with rMenB+OMV NZ compared to MenACWY administered alone, as measured by hSBA GMTs against the N. meningitidis serogroup Men W, at one month after the vaccination with MenACWY (at Day 31).

Comparison groups	MenB+MenACWY Group v MenACWY Group
Number of subjects included in analysis	598
Analysis specification	Pre-specified
Analysis type	
Method	ANOVA
Parameter estimate	GMT Ratio
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.82
upper limit	1.21

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

To demonstrate the non-inferiority of the antibody response to MenACWY given concomitantly with

rMenB+OMV NZ compared to MenACWY administered alone, as measured by hSBA GMTs against the N. meningitidis serogroup Men C, at one month after the vaccination with MenACWY (at Day 31).

Comparison groups	MenB+MenACWY Group v MenACWY Group
Number of subjects included in analysis	598
Analysis specification	Pre-specified
Analysis type	
Method	ANOVA
Parameter estimate	GMT Ratio
Point estimate	1.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.86
upper limit	1.44

Secondary: hSBA GMTs against each of the serogroup B strains in both MenB+MenACWY and MenB Groups after first rMenB+OMV NZ vaccination and between-group GMT ratios

End point title	hSBA GMTs against each of the serogroup B strains in both MenB+MenACWY and MenB Groups after first rMenB+OMV NZ vaccination and between-group GMT ratios[37]

End point description:

hSBA titers were measured by bactericidal activity against N. meningitidis serogroup B indicator strains (M14459 [fHbp], 96217 [NadA], NZ98/254 [PorA] and M13520 [NHBA]) and expressed in GMTs. Analysis was performed on PPS population. Only those participants with data available at specified timepoint were included in analysis.

End point type	Secondary

End point timeframe:

At Day 31 (1 month after first vaccination with rMenB+OMV NZ)

Notes:

[37] - 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: As specified in the Protocol, the analysis assess the imqmune response to rMenB+OMV NZ in healthy subjects 16-18 years of age against N. meningitidis serogroup B test strains M14459 (fHbp), 96217 (NadA), NZ98/254 (PorA) and M07-0241084 (NHBA), at one month after the first vaccination with rMenB+OMV NZ.

End point values	MenB+MenACWY Group	MenB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	294	294		
Units: Titers				
geometric mean (confidence interval 95%)				
fHbp (M14459)	4.3 (3.6 to 5.1)	5.6 (4.7 to 6.7)		
NadA (96217)	45.2 (36.0 to 56.9)	73.4 (58.5 to 91.9)		
PorA (NZ98/254)	4.2 (3.5 to 5.0)	5.6 (4.7 to 6.6)		
NHBA (M13520)	6.4 (5.1 to 8.1)	8.8 (7.0 to 11.1)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

To assess the immune response to rMenB+OMV NZ given concomitantly with MenACWY compared to rMenB+OMV NZ administered alone, measured by hSBA GMTs against N. meningitidis M14459 (fHbp) strain at one month after the fisrt vaccination with rMenB+OMV NZ (at Day 31).

Comparison groups	MenB+MenACWY Group v MenB Group
Number of subjects included in analysis	588
Analysis specification	Pre-specified
Analysis type	
Method	ANOVA
Parameter estimate	GMT Ratio
Point estimate	0.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.64
upper limit	0.91

Statistical analysis title	Statistical Analysis 4

Statistical analysis description:

To assess the immune response to rMenB+OMV NZ given concomitantly with MenACWY compared to rMenB+OMV NZ administered alone, measured by hSBA GMTs against N. meningitidis M13520 (NHBA) at one month after the second vaccination with rMenB+OMV NZ (at Day 31).

Comparison groups	MenB+MenACWY Group v MenB Group
Number of subjects included in analysis	588
Analysis specification	Pre-specified
Analysis type	
Method	ANOVA
Parameter estimate	GMT Ratio
Point estimate	0.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.64
upper limit	0.9

Statistical analysis title	Statistical Analysis 3

Statistical analysis description:

To assess the immune response to rMenB+OMV NZ given concomitantly with MenACWY compared to rMenB+OMV NZ administered alone, measured by hSBA GMTs against N. meningitidis NZ98/254 (PorA) strain at one month after the second vaccination with rMenB+OMV NZ (at Day 31).

Comparison groups	MenB+MenACWY Group v MenB Group

Number of subjects included in analysis	588
Analysis specification	Pre-specified
Analysis type	
Method	ANOVA
Parameter estimate	GMT Ratio
Point estimate	0.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.58
upper limit	0.91

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

To assess the immune response to rMenB+OMV NZ given concomitantly with MenACWY compared to rMenB+OMV NZ administered alone, measured by hSBA GMTs against N. meningitidis 96217 (NadA) strain at one month after the second vaccination with rMenB+OMV NZ (at Day 31).

Comparison groups	MenB+MenACWY Group v MenB Group
Number of subjects included in analysis	588
Analysis specification	Pre-specified
Analysis type	
Method	ANOVA
Parameter estimate	GMT Ratio
Point estimate	0.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.49
upper limit	0.77

Secondary: hSBA Geometric Mean Concentrations (GMCs) measured by ECL against each of the N. meningitidis serogroups after MenACWY vaccination

End point title	hSBA Geometric Mean Concentrations (GMCs) measured by ECL against each of the N. meningitidis serogroups after MenACWY vaccination

End point description:

Immune response to MenACWY given with or without rMenB+OMV NZ, as measured by lectrochemiluminescence-based multiplex (ECL) GMCs against each of the serogroups A, C, W and Y. ECL (validated assay) was used because ELISA is not validated. Analysis was performed on the PPS population, which included participants who received at least 1 dose of the study intervention to which they were randomized and had post-vaccination data available at the specified timepoint minus participants with protocol deviations that led to exclusion from the PPS. 99999" is used as a placeholder value for the results for all the groups since the analysis of final results for these groups is ongoing and will be updated subsequently.

End point type	Secondary

End point timeframe:

At Day 31 (1 month after the vaccination of MenACWY in MenACWY and MenB+MenACWY groups)

End point values	MenB+MenACWY Group	MenB Group	MenACWY Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	310	308	320	
Units: IU/L				
geometric mean (confidence interval 95%)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric mean ratios (GMRs) against each of the N. meningitidis serogroup B strains in both MenB+MenACWY and MenB Groups after the first rMenB+OMV NZ vaccination

End point title	Geometric mean ratios (GMRs) against each of the N. meningitidis serogroup B strains in both MenB+MenACWY and MenB Groups after the first rMenB+OMV NZ vaccination[38]

End point description:

The immune response to rMenB+OMV NZ was measured by bactericidal activity against N. meningitidis serogroup B indicator strains (M14459 [fHbp], 96217 [NadA], NZ98/254 [PorA] and M13520 [NHBA]) in terms of GMRs (after vaccination/baseline). Analysis was performed on PPS population. Only those participants with data available at specified timepoint were included in analysis.

End point type	Secondary

End point timeframe:

At Day 31 (1 month after first rMenB+OMV NZ vaccination) compared to the baseline (Day 1)

Notes:

[38] - 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: As specified in the Protocol, the analysis assess the immune response to rMenB+OMV NZ in healthy subjects 16-18 years of age against N. meningitidis serogroup B test strains M14459 (fHbp), 96217 (NadA), NZ98/254 (PorA) and M07-0241084 (NHBA), at one month after the first vaccination with rMenB+OMV NZ.

End point values	MenB+MenACWY Group	MenB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	294	294		
Units: Ratio				
geometric mean (confidence interval 95%)				
fHbp (M14459)	1.6 (1.4 to 1.9)	2.0 (1.7 to 2.4)		
NadA (96217)	5.9 (4.7 to 7.4)	9.3 (7.5 to 11.6)		
PorA (NZ98/254)	1.4 (1.2 to 1.6)	1.8 (1.5 to 2.1)		
NHBA (M13520)	1.8 (1.5 to 2.2)	2.3 (1.9 to 2.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: GMRs against each of the N. meningitidis serogroup B strains in both MenB+MenACWY and MenB Groups after the second rMenB+OMV NZ vaccination

End point title	GMRs against each of the N. meningitidis serogroup B strains in both MenB+MenACWY and MenB Groups after the second rMenB+OMV NZ vaccination[39]

End point description:

The immune response to rMenB+OMV NZ was measured by bactericidal activity against N. meningitidis serogroup B indicator strains (M14459 [fHbp], 96217 [NadA], NZ98/254 [PorA] and M13520 [NHBA]) in terms of GMRs (after vaccination/baseline). Analysis was performed on PPS population. Only those participants with data available at specified timepoint were included in analysis.

End point type	Secondary

End point timeframe:

At Day 91 (1 month after the second rMenB+OMV NZ vaccination) compared to the baseline (Day 1)

Notes:

[39] - 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: As specified in the Protocol, the analysis assess the imqmune response to rMenB+OMV NZ in healthy subjects 16-18 years of age against N. meningitidis serogroup B test strains M14459 (fHbp), 96217 (NadA), NZ98/254 (PorA) and M07-0241084 (NHBA), at one month after the second vaccination with rMenB+OMV NZ.

End point values	MenB+MenACWY Group	MenB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	274	267		
Units: Ratio				
geometric mean (confidence interval 95%)				
fHbp (M14459)	6.4 (5.5 to 7.5)	7.0 (5.9 to 8.1)		
NadA (96217)	30.7 (25.8 to 36.6)	35.1 (29.5 to 41.7)		
PorA (NZ98/254)	6.0 (5.0 to 7.2)	6.9 (5.8 to 8.3)		
NHBA (M13520)	5.2 (4.4 to 6.2)	5.6 (4.7 to 6.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with hSBA titers >= lower limit of quantitation (LLOQ) for each and all serogroup B test strains in both MenB+MenACWY and MenB Groups after the first rMenB+OMV NZ vaccination

End point title	Percentage of participants with hSBA titers >= lower limit of quantitation (LLOQ) for each and all serogroup B test strains in both MenB+MenACWY and MenB Groups after the first rMenB+OMV NZ vaccination[40]

End point description:

The immune response to rMenB+OMV NZ vaccine is evaluated by measuring bactericidal activity in terms of participants with hSBA titers >= LLOQ against N. meningitidis serogroup B test strains (M14459 [fHbp], 96217 [NadA], NZ98/254 [PorA] and M13520 [NHBA]). Analysis was performed on PPS population. Only those participants with data available at specified timepoint were included in analysis.

End point type	Secondary

End point timeframe:

At Day 31 (one month after the first rMenB+OMV NZ vaccination)

Notes:

[40] - 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: As specified in the Protocol, the analysis assess the imqmune response to rMenB+OMV NZ in healthy subjects 16-18 years of age against N. meningitidis serogroup B test strains M14459 (fHbp), 96217 (NadA), NZ98/254 (PorA) and M07-0241084 (NHBA), at one month after the first vaccination with rMenB+OMV NZ.

End point values	MenB+MenACWY Group	MenB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	294	294		
Units: Percentage of participants				
number (confidence interval 95%)				
fHbp (M14459)	32.3 (27.0 to 38.0)	44.9 (39.1 to 50.8)		
NadA (96217)	77.9 (72.7 to 82.5)	85.7 (81.2 to 89.5)		
PorA (NZ98/254)	21.1 (16.6 to 26.2)	30.4 (25.2 to 36.0)		
NHBA (M13520)	37.1 (31.5 to 42.9)	44.4 (38.6 to 50.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with hSBA titers >= LLOQ for each and all of the serogroup B test strains in both MenB+MenACWY and MenB Groups after the second rMenB+OMV NZ vaccination

End point title	Percentage of participants with hSBA titers >= LLOQ for each and all of the serogroup B test strains in both MenB+MenACWY and MenB Groups after the second rMenB+OMV NZ vaccination[41]

End point description:

The immune response to rMenB+OMV NZ vaccine is evaluated by measuring bactericidal activity in terms of participants with hSBA titers >= LLOQ against N. meningitidis serogroup B test strains (M14459 [fHbp], 96217 [NadA], NZ98/254 [PorA] and M13520 [NHBA]). Analysis was performed on PPS population. Only those participants with data available at specified timepoint were included in analysis.

End point type	Secondary

End point timeframe:

At Day 91 (1 month after the second rMenB+OMV NZ vaccination)

Notes:

[41] - 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: As specified in the Protocol, the analysis assess the imqmune response to rMenB+OMV NZ in healthy subjects 16-18 years of age against N. meningitidis serogroup B test strains M14459 (fHbp), 96217 (NadA), NZ98/254 (PorA) and M07-0241084 (NHBA), at one month after the second vaccination with rMenB+OMV NZ.

End point values	MenB+MenACWY Group	MenB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	274	267		
Units: Percentage of participants				
number (confidence interval 95%)				
fHbp (M14459)	92.3 (88.5 to 95.2)	92.5 (88.6 to 95.3)		
NadA (96217)	99.6 (98.0 to 100)	99.6 (97.9 to 100)		
PorA (NZ98/254)	83.2 (78.2 to 87.4)	85.0 (80.1 to 89.0)		
NHBA (M13520)	84.2 (79.4 to 88.4)	90.2 (86.0 to 93.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with 4-fold increase in hSBA titers relative to baseline in both MenB+MenACWY and MenB Groups after the first rMenB+OMV NZ vaccination

End point title	Percentage of participants with 4-fold increase in hSBA titers relative to baseline in both MenB+MenACWY and MenB Groups after the first rMenB+OMV NZ vaccination[42]

End point description:

The immune response to rMenB+OMV NZ vaccine is evaluated by measuring bactericidal activity against each of N. meningitidis serogroup B test strains (M14459 [fHbp], 96217 [NadA], NZ98/254 [PorA] and M13520 [NHBA]) in terms of the Four-fold increase defined as: - For a pre-vaccination titer < limit of detection (LOD), a post-vaccination titer of >= 4-fold the LOD or >= LLOQ, whichever is greater, - For a pre-vaccination titer >= LOD but <LLOQ, a post vaccination titer of at least 4-fold the LLOQ, - For a pre-vaccination titer >= LLOQ, a post vaccination titer of at least 4-fold the pre-vaccination titer. Analysis was performed on PPS population. Only those participants with data available at specified timepoint were included in analysis.

End point type	Secondary

End point timeframe:

At 1 month after the first rMenB+OMV NZ vaccination (i.e at Day 31) relative to baseline (i.e. Day 1)

Notes:

[42] - 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: As specified in the Protocol, the analysis assess the imqmune response to rMenB+OMV NZ in healthy subjects 16-18 years of age against N. meningitidis serogroup B test strains M14459 (fHbp), 96217 (NadA), NZ98/254 (PorA) and M07-0241084 (NHBA), at one month after the first vaccination with rMenB+OMV NZ.

End point values	MenB+MenACWY Group	MenB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	293	293		
Units: Percentage of participants				
number (confidence interval 95%)				
fHbp (M14459)	14.7 (10.8 to 19.3)	21.0 (16.4 to 26.1)		
NadA (96217)	68.9 (63.3 to 74.2)	78.4 (73.3 to 83.0)		

PorA (NZ98/254)	8.9 (5.9 to 12.7)	16.4 (12.4 to 21.2)		
NHBA (M13520)	17.4 (13.2 to 22.2)	25.3 (20.4 to 30.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with hSBA titers >=LLOQ for each of the serogroup A, C, W and Y in both MenB+MenACWY and MenACWY Groups after MenACWY vaccination

End point title	Percentage of participants with hSBA titers >=LLOQ for each of the serogroup A, C, W and Y in both MenB+MenACWY and MenACWY Groups after MenACWY vaccination[43]

End point description:

The immune response to MenACWY vaccines is expressed in terms of percentage of participants with hSBA titers >=LLOQ for each of the serogroup Men A, Men C, Men W and Men Y. Analysis was performed on PPS population. Only those participants with data available at specified timepoint were included in analysis.

End point type	Secondary

End point timeframe:

At baseline (Day 1) and at one month after the MenACWY vaccination (i.e. Day 31)

Notes:

[43] - 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: As specified in the Protocol, the analysis assesses the immune response to MenACWY in healthy subjects 16-18 years of age against each of the serogroups A, C, W and Y, at one month after the (study) vaccination with MenACWY.

End point values	MenB+MenACWY Group	MenACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	295	303		
Units: Percentage of participants				
number (confidence interval 95%)				
Men A, Baseline (Day 1)	28.1 (22.8 to 33.9)	30.0 (24.7 to 35.9)		
Men A, Day 31	99.7 (98.1 to 100)	99.3 (97.5 to 99.9)		
Men C, Baseline (Day 1)	46.3 (40.5 to 52.1)	44.4 (38.7 to 50.3)		
Men C, Day 31	99.0 (97.1 to 99.8)	98.7 (96.6 to 99.6)		
Men W, Baseline (Day 1)	27.4 (22.4 to 32.9)	28.4 (23.3 to 34.0)		
Men W, Day 31	100 (98.8 to 100)	100 (98.8 to 100)		
Men Y, Baseline (Day 1)	23.4 (18.6 to 28.7)	23.0 (18.3 to 28.2)		
Men Y, Day 31	99.7 (98.1 to 100)	99.7 (98.2 to 100)		

Statistical analyses

No statistical analyses for this end point

Secondary: GMRs against each of the N. meningitidis serogroup Men A, Men C, Men W and Men Y in both MenB+MenACWY and MenACWY Groups after MenACWY vaccination

End point title	GMRs against each of the N. meningitidis serogroup Men A, Men C, Men W and Men Y in both MenB+MenACWY and MenACWY Groups after MenACWY vaccination[44]

End point description:

Immune response to MenACWY given with or without rMenB+OMV NZ was measured by bactericidal activity against the four serogroups Men A, Men C, Men W and Men Y in terms of GMRs at one month after MenACWY vaccination compared to the baseline at Day 1/Month 0. GMR was measured within-group. Analysis was performed on PPS population. Only those participants with data available at specified timepoint were included in analysis.

End point type	Secondary

End point timeframe:

At 1 month after MenACWY vaccination (i.e.at Day 31) compared to the baseline (Day 1)

Notes:

[44] - 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: As specified in the Protocol, the analysis assesses the immune response to MenACWY in healthy subjects 16-18 years of age against each of the serogroups A, C, W and Y, at one month after the (study) vaccination with MenACWY.

End point values	MenB+MenACWY Group	MenACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	295	303		
Units: Ratio				
geometric mean (confidence interval 95%)				
Men A	150.2 (120.1 to 187.8)	145.0 (115.4 to 182.2)		
Men C	130.0 (97.7 to 173.1)	131.9 (98.8 to 176.1)		
Men W	294.2 (229.0 to 378.1)	279.3 (216.6 to 360.1)		
Men Y	324.3 (252.2 to 417.0)	300.0 (232.9 to 386.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with 4-fold increase in hSBA titers against

each of the N. meningitidis serogroup Men A, Men C, Men W and Men Y relative to baseline in both MenB+MenACWY and MenACWY Groups after MenACWY vaccination

End point title	Percentage of participants with 4-fold increase in hSBA titers against each of the N. meningitidis serogroup Men A, Men C, Men W and Men Y relative to baseline in both MenB+MenACWY and MenACWY Groups after MenACWY vaccination[45]

End point description:

The immune response to MenACWY vaccine is evaluated by measuring percentage of participants with 4-fold increase for the four serogroups Men A, Men C, Men W and Men Y. The Four-fold increase defined as: - For a pre-vaccination titer <LOD, a post-vaccination titer of >= 4-fold the LOD or >= LLOQ, whichever is greater, - For a pre-vaccination titer >=LOD but <LLOQ, a post vaccination titer of at least 4-fold the LLOQ, - For a pre-vaccination titer >= LLOQ, a post vaccination titer of at least 4-fold the pre-vaccination titer. Analysis was performed on PPS population. Only those participants with data available at specified timepoint were included in analysis.

End point type	Secondary

End point timeframe:

At 1 month after MenACWY vaccination (i.e at Day 31) relative to baseline (i.e. Day 1)

Notes:

[45] - 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: As specified in the Protocol, the analysis assesses the immune response to MenACWY in healthy subjects 16-18 years of age against each of the serogroups A, C, W and Y, at one month after the (study) vaccination with MenACWY.

End point values	MenB+MenACWY Group	MenACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	293	296		
Units: Percentage of participants				
number (confidence interval 95%)				
Men A	98.5 (96.1 to 99.6)	98.1 (95.6 to 99.4)		
Men C	95.2 (92.1 to 97.4)	95.6 (92.6 to 97.6)		
Men W	98.6 (96.5 to 99.6)	97.9 (95.6 to 99.2)		
Men Y	98.6 (96.5 to 99.6)	98.3 (96.1 to 99.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with 4-fold increase in hSBA titers relative to baseline in both MenB+MenACWY and MenB Groups after the second rMenB+OMV NZ vaccination

End point title	Percentage of participants with 4-fold increase in hSBA titers relative to baseline in both MenB+MenACWY and MenB Groups after the second rMenB+OMV NZ vaccination[46]

End point description:

The immune response to rMenB+OMV NZ vaccine is evaluated by measuring bactericidal activity against each of the N. meningitidis serogroup B test strains (M14459 [fHbp], 96217 [NadA], NZ98/254 [PorA] and M13520 [NHBA]) in terms of the Four-fold increase defined as: - For a pre-vaccination titer <LOD, a post-vaccination titer of >= 4-fold the LOD or >= LLOQ, whichever is greater, - For a pre-vaccination titer >=LOD but <LLOQ, a post vaccination titer of at least 4-fold the LLOQ, - For a pre-vaccination titer >=LLOQ, a post vaccination titer of at least 4-fold the pre-vaccination titer. Analysis was performed on

PPS population. Only those participants with data available at specified timepoint were included in analysis.

End point type	Secondary

End point timeframe:

At 1 month after the second rMenB+OMV vaccination (i.e at Day 91) relative to baseline (i.e. Day 1)

Notes:

[46] - 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: As specified in the Protocol, the analysis assess the imqmune response to rMenB+OMV NZ in healthy subjects 16-18 years of age against N. meningitidis serogroup B test strains M14459 (fHbp), 96217 (NadA), NZ98/254 (PorA) and M07-0241084 (NHBA), at one month after the second vaccination with rMenB+OMV NZ.

End point values	MenB+MenACWY Group	MenB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	273	266		
Units: Percentage of participants				
number (confidence interval 95%)				
fHbp (M14459)	57.1 (51.0 to 63.1)	64.6 (58.5 to 70.4)		
NadA (96217)	96.0 (92.9 to 98.0)	98.9 (96.7 to 99.8)		
PorA (NZ98/254)	51.5 (45.4 to 57.5)	56.6 (50.4 to 62.7)		
NHBA (M13520)	55.1 (49.0 to 61.2)	53.0 (46.8 to 59.1)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited AEs: within 7 days post-vaccination. Unsolicited AEs: within 30 days post-vaccination. All-cause mortality,SAEs,MAAEs, AEs leading to withdrawal, and AESIs: monitored from Day 1 to study end at Day 271 or Day 451, depending on participation date

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27.0

Reporting groups

Reporting group title	MenB+MenACWY Group

Reporting group description:

Participants received 1 dose of rMenB+OMV NZ vaccine administered concomitantly with 1 dose of MenACWY vaccine, as separate injections in each arm at Day 1, 1 dose of rMenB+OMV NZ vaccine at Day 61 and 1 dose of placebo at Day 91.

Reporting group title	MenACWY Group

Reporting group description:

Participants received 1 dose of MenACWY vaccine administered concomitantly with 1 dose of placebo, as separate injections in each arm at Day1, 1 dose of rMenB+OMV NZ vaccine each administered at Day 61 and at Day 91.

Reporting group title	MenB Group

Reporting group description:

Participants received 1 dose of rMenB+OMV NZ vaccine administered concomitantly with 1 dose of placebo, as separate injections in each arm at Day 1, 1 dose of rMenB+OMV NZ vaccine at Day 61 and 1 dose of MenACWY at Day 91.

Serious adverse events	MenB+MenACWY Group	MenACWY Group	MenB Group
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 310 (0.65%)	7 / 320 (2.19%)	4 / 308 (1.30%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Lumbar vertebral fracture			
subjects affected / exposed	1 / 310 (0.32%)	0 / 320 (0.00%)	0 / 308 (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
Fibula fracture			
subjects affected / exposed	0 / 310 (0.00%)	1 / 320 (0.31%)	0 / 308 (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
Pregnancy, puerperium and perinatal			

conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 310 (0.00%)	1 / 320 (0.31%)	0 / 308 (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
Psychiatric disorders			
Adjustment disorder with depressed mood			
subjects affected / exposed	0 / 310 (0.00%)	1 / 320 (0.31%)	0 / 308 (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
Depression			
subjects affected / exposed	1 / 310 (0.32%)	0 / 320 (0.00%)	0 / 308 (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
Drug abuse			
subjects affected / exposed	0 / 310 (0.00%)	1 / 320 (0.31%)	0 / 308 (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
Major depression			
subjects affected / exposed	0 / 310 (0.00%)	1 / 320 (0.31%)	0 / 308 (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
Suicidal ideation			
subjects affected / exposed	0 / 310 (0.00%)	0 / 320 (0.00%)	2 / 308 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	0 / 310 (0.00%)	1 / 320 (0.31%)	0 / 308 (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
Rhabdomyolysis			

subjects affected / exposed	0 / 310 (0.00%)	1 / 320 (0.31%)	0 / 308 (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			
Appendicitis			
subjects affected / exposed	0 / 310 (0.00%)	0 / 320 (0.00%)	1 / 308 (0.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	0 / 310 (0.00%)	0 / 320 (0.00%)	1 / 308 (0.32%)
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: 0 %

Non-serious adverse events	MenB+MenACWY Group	MenACWY Group	MenB Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	293 / 310 (94.52%)	289 / 320 (90.31%)	293 / 308 (95.13%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Melanocytic naevus			
subjects affected / exposed	0 / 310 (0.00%)	1 / 320 (0.31%)	0 / 308 (0.00%)
occurrences (all)	0	1	0
Vascular disorders			
Pallor			
subjects affected / exposed	1 / 310 (0.32%)	0 / 320 (0.00%)	0 / 308 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Feeling of body temperature change			
subjects affected / exposed	0 / 310 (0.00%)	1 / 320 (0.31%)	0 / 308 (0.00%)
occurrences (all)	0	1	0
Fatigue			
subjects affected / exposed	152 / 310 (49.03%)	159 / 320 (49.69%)	160 / 308 (51.95%)
occurrences (all)	265	303	306
Chills			

subjects affected / exposed	2 / 310 (0.65%)	3 / 320 (0.94%)	2 / 308 (0.65%)
occurrences (all)	2	3	3
Chest pain			
subjects affected / exposed	0 / 310 (0.00%)	1 / 320 (0.31%)	1 / 308 (0.32%)
occurrences (all)	0	1	1
Chest discomfort			
subjects affected / exposed	0 / 310 (0.00%)	0 / 320 (0.00%)	1 / 308 (0.32%)
occurrences (all)	0	0	1
Administration site swelling			
subjects affected / exposed	31 / 310 (10.00%)	26 / 320 (8.13%)	32 / 308 (10.39%)
occurrences (all)	38	33	44
Administration site pain			
subjects affected / exposed	281 / 310 (90.65%)	268 / 320 (83.75%)	282 / 308 (91.56%)
occurrences (all)	589	629	597
Administration site induration			
subjects affected / exposed	31 / 310 (10.00%)	25 / 320 (7.81%)	35 / 308 (11.36%)
occurrences (all)	46	33	56
Administration site erythema			
subjects affected / exposed	28 / 310 (9.03%)	28 / 320 (8.75%)	31 / 308 (10.06%)
occurrences (all)	39	30	37
Swelling			
subjects affected / exposed	0 / 310 (0.00%)	1 / 320 (0.31%)	1 / 308 (0.32%)
occurrences (all)	0	1	1
Peripheral swelling			
subjects affected / exposed	0 / 310 (0.00%)	1 / 320 (0.31%)	0 / 308 (0.00%)
occurrences (all)	0	1	0
Pain			
subjects affected / exposed	1 / 310 (0.32%)	0 / 320 (0.00%)	1 / 308 (0.32%)
occurrences (all)	1	0	1
Malaise			
subjects affected / exposed	2 / 310 (0.65%)	0 / 320 (0.00%)	0 / 308 (0.00%)
occurrences (all)	2	0	0
Injection site swelling			
subjects affected / exposed	1 / 310 (0.32%)	0 / 320 (0.00%)	0 / 308 (0.00%)
occurrences (all)	1	0	0
Injection site reaction			

subjects affected / exposed	1 / 310 (0.32%)	1 / 320 (0.31%)	0 / 308 (0.00%)
occurrences (all)	1	1	0
Injection site pruritus			
subjects affected / exposed	0 / 310 (0.00%)	0 / 320 (0.00%)	1 / 308 (0.32%)
occurrences (all)	0	0	1
Injection site pain			
subjects affected / exposed	1 / 310 (0.32%)	0 / 320 (0.00%)	1 / 308 (0.32%)
occurrences (all)	1	0	1
Injection site hypoaesthesia			
subjects affected / exposed	0 / 310 (0.00%)	1 / 320 (0.31%)	0 / 308 (0.00%)
occurrences (all)	0	1	0
Injection site bruising			
subjects affected / exposed	3 / 310 (0.97%)	0 / 320 (0.00%)	1 / 308 (0.32%)
occurrences (all)	3	0	2
Influenza like illness			
subjects affected / exposed	1 / 310 (0.32%)	0 / 320 (0.00%)	2 / 308 (0.65%)
occurrences (all)	1	0	2
Induration			
subjects affected / exposed	0 / 310 (0.00%)	1 / 320 (0.31%)	0 / 308 (0.00%)
occurrences (all)	0	1	0
Vaccination site bruising			
subjects affected / exposed	0 / 310 (0.00%)	0 / 320 (0.00%)	1 / 308 (0.32%)
occurrences (all)	0	0	1
Vaccination site erythema			
subjects affected / exposed	0 / 310 (0.00%)	1 / 320 (0.31%)	0 / 308 (0.00%)
occurrences (all)	0	1	0
Vaccination site rash			
subjects affected / exposed	1 / 310 (0.32%)	0 / 320 (0.00%)	0 / 308 (0.00%)
occurrences (all)	1	0	0
Vaccination site swelling			
subjects affected / exposed	0 / 310 (0.00%)	1 / 320 (0.31%)	0 / 308 (0.00%)
occurrences (all)	0	1	0
Pyrexia			
subjects affected / exposed	14 / 310 (4.52%)	19 / 320 (5.94%)	23 / 308 (7.47%)
occurrences (all)	17	21	26
Immune system disorders			

Multiple allergies			
subjects affected / exposed	0 / 310 (0.00%)	1 / 320 (0.31%)	0 / 308 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	5 / 310 (1.61%)	5 / 320 (1.56%)	2 / 308 (0.65%)
occurrences (all)	7	5	2
Abnormal uterine bleeding			
subjects affected / exposed	2 / 310 (0.65%)	0 / 320 (0.00%)	2 / 308 (0.65%)
occurrences (all)	2	0	2
Varicocele			
subjects affected / exposed	1 / 310 (0.32%)	0 / 320 (0.00%)	0 / 308 (0.00%)
occurrences (all)	1	0	0
Vaginal discharge			
subjects affected / exposed	0 / 310 (0.00%)	0 / 320 (0.00%)	1 / 308 (0.32%)
occurrences (all)	0	0	1
Pelvic pain			
subjects affected / exposed	0 / 310 (0.00%)	1 / 320 (0.31%)	0 / 308 (0.00%)
occurrences (all)	0	1	0
Heavy menstrual bleeding			
subjects affected / exposed	0 / 310 (0.00%)	1 / 320 (0.31%)	0 / 308 (0.00%)
occurrences (all)	0	1	0
Gynaecomastia			
subjects affected / exposed	0 / 310 (0.00%)	1 / 320 (0.31%)	0 / 308 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 310 (0.32%)	1 / 320 (0.31%)	1 / 308 (0.32%)
occurrences (all)	1	1	1
Cough			
subjects affected / exposed	1 / 310 (0.32%)	8 / 320 (2.50%)	3 / 308 (0.97%)
occurrences (all)	1	8	3
Upper respiratory tract congestion			
subjects affected / exposed	0 / 310 (0.00%)	0 / 320 (0.00%)	1 / 308 (0.32%)
occurrences (all)	0	0	1
Throat irritation			

subjects affected / exposed	1 / 310 (0.32%)	0 / 320 (0.00%)	0 / 308 (0.00%)
occurrences (all)	1	0	0
Sneezing			
subjects affected / exposed	0 / 310 (0.00%)	0 / 320 (0.00%)	1 / 308 (0.32%)
occurrences (all)	0	0	1
Sinus congestion			
subjects affected / exposed	2 / 310 (0.65%)	0 / 320 (0.00%)	1 / 308 (0.32%)
occurrences (all)	2	0	1
Rhinorrhoea			
subjects affected / exposed	1 / 310 (0.32%)	3 / 320 (0.94%)	1 / 308 (0.32%)
occurrences (all)	1	3	1
Rhinitis allergic			
subjects affected / exposed	0 / 310 (0.00%)	1 / 320 (0.31%)	0 / 308 (0.00%)
occurrences (all)	0	1	0
Respiratory symptom			
subjects affected / exposed	0 / 310 (0.00%)	0 / 320 (0.00%)	1 / 308 (0.32%)
occurrences (all)	0	0	1
Respiratory disorder			
subjects affected / exposed	0 / 310 (0.00%)	0 / 320 (0.00%)	1 / 308 (0.32%)
occurrences (all)	0	0	1
Oropharyngeal pain			
subjects affected / exposed	13 / 310 (4.19%)	10 / 320 (3.13%)	11 / 308 (3.57%)
occurrences (all)	13	10	11
Nasal congestion			
subjects affected / exposed	7 / 310 (2.26%)	5 / 320 (1.56%)	3 / 308 (0.97%)
occurrences (all)	7	5	3
Epistaxis			
subjects affected / exposed	0 / 310 (0.00%)	1 / 320 (0.31%)	0 / 308 (0.00%)
occurrences (all)	0	1	0
Dyspnoea			
subjects affected / exposed	1 / 310 (0.32%)	1 / 320 (0.31%)	1 / 308 (0.32%)
occurrences (all)	1	1	1
Dysphonia			
subjects affected / exposed	0 / 310 (0.00%)	0 / 320 (0.00%)	1 / 308 (0.32%)
occurrences (all)	0	0	1
Wheezing			

subjects affected / exposed	0 / 310 (0.00%)	0 / 320 (0.00%)	1 / 308 (0.32%)
occurrences (all)	0	0	1
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 310 (0.00%)	1 / 320 (0.31%)	0 / 308 (0.00%)
occurrences (all)	0	1	0
Depression			
subjects affected / exposed	2 / 310 (0.65%)	1 / 320 (0.31%)	2 / 308 (0.65%)
occurrences (all)	2	1	2
Generalised anxiety disorder			
subjects affected / exposed	0 / 310 (0.00%)	0 / 320 (0.00%)	1 / 308 (0.32%)
occurrences (all)	0	0	1
Intentional self-injury			
subjects affected / exposed	1 / 310 (0.32%)	0 / 320 (0.00%)	0 / 308 (0.00%)
occurrences (all)	1	0	0
Investigations			
Arthroscopy			
subjects affected / exposed	1 / 310 (0.32%)	0 / 320 (0.00%)	0 / 308 (0.00%)
occurrences (all)	1	0	0
Blood cholesterol increased			
subjects affected / exposed	0 / 310 (0.00%)	1 / 320 (0.31%)	0 / 308 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Breast procedural complication			
subjects affected / exposed	1 / 310 (0.32%)	0 / 320 (0.00%)	0 / 308 (0.00%)
occurrences (all)	1	0	0
Abdominal injury			
subjects affected / exposed	0 / 310 (0.00%)	0 / 320 (0.00%)	1 / 308 (0.32%)
occurrences (all)	0	0	1
Joint injury			
subjects affected / exposed	1 / 310 (0.32%)	0 / 320 (0.00%)	0 / 308 (0.00%)
occurrences (all)	1	0	0
Head injury			
subjects affected / exposed	0 / 310 (0.00%)	0 / 320 (0.00%)	1 / 308 (0.32%)
occurrences (all)	0	0	1
Foot fracture			

subjects affected / exposed	0 / 310 (0.00%)	0 / 320 (0.00%)	1 / 308 (0.32%)
occurrences (all)	0	0	1
Fibula fracture			
subjects affected / exposed	0 / 310 (0.00%)	0 / 320 (0.00%)	1 / 308 (0.32%)
occurrences (all)	0	0	1
Face injury			
subjects affected / exposed	1 / 310 (0.32%)	0 / 320 (0.00%)	0 / 308 (0.00%)
occurrences (all)	1	0	0
Eye injury			
subjects affected / exposed	0 / 310 (0.00%)	1 / 320 (0.31%)	0 / 308 (0.00%)
occurrences (all)	0	1	0
Distal clavicular osteolysis			
subjects affected / exposed	1 / 310 (0.32%)	0 / 320 (0.00%)	0 / 308 (0.00%)
occurrences (all)	1	0	0
Contusion			
subjects affected / exposed	0 / 310 (0.00%)	3 / 320 (0.94%)	1 / 308 (0.32%)
occurrences (all)	0	3	1
Concussion			
subjects affected / exposed	2 / 310 (0.65%)	0 / 320 (0.00%)	3 / 308 (0.97%)
occurrences (all)	2	0	3
Ligament injury			
subjects affected / exposed	0 / 310 (0.00%)	1 / 320 (0.31%)	0 / 308 (0.00%)
occurrences (all)	0	1	0
Seroma			
subjects affected / exposed	1 / 310 (0.32%)	0 / 320 (0.00%)	0 / 308 (0.00%)
occurrences (all)	1	0	0
Scar			
subjects affected / exposed	1 / 310 (0.32%)	0 / 320 (0.00%)	0 / 308 (0.00%)
occurrences (all)	1	0	0
Procedural pain			
subjects affected / exposed	1 / 310 (0.32%)	1 / 320 (0.31%)	2 / 308 (0.65%)
occurrences (all)	1	1	2
Open globe injury			
subjects affected / exposed	0 / 310 (0.00%)	1 / 320 (0.31%)	0 / 308 (0.00%)
occurrences (all)	0	1	0
Muscle strain			

subjects affected / exposed	1 / 310 (0.32%)	1 / 320 (0.31%)	1 / 308 (0.32%)
occurrences (all)	1	1	1
Lip injury			
subjects affected / exposed	0 / 310 (0.00%)	0 / 320 (0.00%)	1 / 308 (0.32%)
occurrences (all)	0	0	1
Limb injury			
subjects affected / exposed	0 / 310 (0.00%)	0 / 320 (0.00%)	4 / 308 (1.30%)
occurrences (all)	0	0	5
Ligament sprain			
subjects affected / exposed	0 / 310 (0.00%)	3 / 320 (0.94%)	1 / 308 (0.32%)
occurrences (all)	0	3	1
Ligament rupture			
subjects affected / exposed	0 / 310 (0.00%)	0 / 320 (0.00%)	1 / 308 (0.32%)
occurrences (all)	0	0	1
Skin laceration			
subjects affected / exposed	1 / 310 (0.32%)	0 / 320 (0.00%)	1 / 308 (0.32%)
occurrences (all)	1	0	1
Thermal burn			
subjects affected / exposed	1 / 310 (0.32%)	0 / 320 (0.00%)	0 / 308 (0.00%)
occurrences (all)	1	0	0
Torus fracture			
subjects affected / exposed	1 / 310 (0.32%)	0 / 320 (0.00%)	0 / 308 (0.00%)
occurrences (all)	1	0	0
Vulvovaginal injury			
subjects affected / exposed	0 / 310 (0.00%)	0 / 320 (0.00%)	1 / 308 (0.32%)
occurrences (all)	0	0	1
Suture related complication			
subjects affected / exposed	1 / 310 (0.32%)	0 / 320 (0.00%)	0 / 308 (0.00%)
occurrences (all)	1	0	0
Congenital, familial and genetic disorders			
Os trigonum			
subjects affected / exposed	1 / 310 (0.32%)	0 / 320 (0.00%)	0 / 308 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			

Tachycardia			
subjects affected / exposed	0 / 310 (0.00%)	1 / 320 (0.31%)	0 / 308 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 310 (0.32%)	2 / 320 (0.63%)	3 / 308 (0.97%)
occurrences (all)	1	2	3
Headache			
subjects affected / exposed	178 / 310 (57.42%)	185 / 320 (57.81%)	185 / 308 (60.06%)
occurrences (all)	320	345	317
Migraine			
subjects affected / exposed	1 / 310 (0.32%)	0 / 320 (0.00%)	1 / 308 (0.32%)
occurrences (all)	1	0	1
Paraesthesia			
subjects affected / exposed	1 / 310 (0.32%)	0 / 320 (0.00%)	0 / 308 (0.00%)
occurrences (all)	1	0	0
Sciatica			
subjects affected / exposed	1 / 310 (0.32%)	0 / 320 (0.00%)	0 / 308 (0.00%)
occurrences (all)	1	0	0
Sinus headache			
subjects affected / exposed	0 / 310 (0.00%)	0 / 320 (0.00%)	1 / 308 (0.32%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	2 / 310 (0.65%)	2 / 320 (0.63%)	0 / 308 (0.00%)
occurrences (all)	2	2	0
Neutropenia			
subjects affected / exposed	0 / 310 (0.00%)	0 / 320 (0.00%)	1 / 308 (0.32%)
occurrences (all)	0	0	1
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 310 (0.00%)	3 / 320 (0.94%)	0 / 308 (0.00%)
occurrences (all)	0	3	0
Cerumen impaction			
subjects affected / exposed	0 / 310 (0.00%)	1 / 320 (0.31%)	1 / 308 (0.32%)
occurrences (all)	0	1	1
Tympanic membrane perforation			

subjects affected / exposed	0 / 310 (0.00%)	0 / 320 (0.00%)	1 / 308 (0.32%)
occurrences (all)	0	0	1
Eustachian tube dysfunction			
subjects affected / exposed	1 / 310 (0.32%)	1 / 320 (0.31%)	0 / 308 (0.00%)
occurrences (all)	1	1	0
Eye disorders			
Photophobia			
subjects affected / exposed	1 / 310 (0.32%)	0 / 320 (0.00%)	0 / 308 (0.00%)
occurrences (all)	1	0	0
Ocular hyperaemia			
subjects affected / exposed	0 / 310 (0.00%)	1 / 320 (0.31%)	0 / 308 (0.00%)
occurrences (all)	0	1	0
Myopia			
subjects affected / exposed	0 / 310 (0.00%)	0 / 320 (0.00%)	1 / 308 (0.32%)
occurrences (all)	0	0	1
Episcleritis			
subjects affected / exposed	0 / 310 (0.00%)	1 / 320 (0.31%)	0 / 308 (0.00%)
occurrences (all)	0	1	0
Lacrimation increased			
subjects affected / exposed	1 / 310 (0.32%)	0 / 320 (0.00%)	0 / 308 (0.00%)
occurrences (all)	1	0	0
Astigmatism			
subjects affected / exposed	0 / 310 (0.00%)	0 / 320 (0.00%)	1 / 308 (0.32%)
occurrences (all)	0	0	1
Blepharitis			
subjects affected / exposed	0 / 310 (0.00%)	1 / 320 (0.31%)	0 / 308 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	0 / 310 (0.00%)	0 / 320 (0.00%)	1 / 308 (0.32%)
occurrences (all)	0	0	1
Cheilitis			
subjects affected / exposed	0 / 310 (0.00%)	0 / 320 (0.00%)	1 / 308 (0.32%)
occurrences (all)	0	0	1
Aphthous ulcer			

subjects affected / exposed	0 / 310 (0.00%)	1 / 320 (0.31%)	0 / 308 (0.00%)
occurrences (all)	0	1	0
Abdominal pain upper			
subjects affected / exposed	0 / 310 (0.00%)	5 / 320 (1.56%)	4 / 308 (1.30%)
occurrences (all)	0	5	5
Abdominal pain			
subjects affected / exposed	2 / 310 (0.65%)	1 / 320 (0.31%)	1 / 308 (0.32%)
occurrences (all)	2	1	1
Abdominal discomfort			
subjects affected / exposed	1 / 310 (0.32%)	0 / 320 (0.00%)	2 / 308 (0.65%)
occurrences (all)	1	0	2
Vomiting			
subjects affected / exposed	4 / 310 (1.29%)	6 / 320 (1.88%)	3 / 308 (0.97%)
occurrences (all)	4	6	3
Salivary gland mucocoele			
subjects affected / exposed	1 / 310 (0.32%)	0 / 320 (0.00%)	0 / 308 (0.00%)
occurrences (all)	1	0	0
Tooth impacted			
subjects affected / exposed	1 / 310 (0.32%)	2 / 320 (0.63%)	0 / 308 (0.00%)
occurrences (all)	1	2	0
Toothache			
subjects affected / exposed	5 / 310 (1.61%)	1 / 320 (0.31%)	0 / 308 (0.00%)
occurrences (all)	5	1	0
Nausea			
subjects affected / exposed	74 / 310 (23.87%)	94 / 320 (29.38%)	90 / 308 (29.22%)
occurrences (all)	105	132	119
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 310 (0.00%)	1 / 320 (0.31%)	0 / 308 (0.00%)
occurrences (all)	0	1	0
Dyspepsia			
subjects affected / exposed	0 / 310 (0.00%)	1 / 320 (0.31%)	0 / 308 (0.00%)
occurrences (all)	0	1	0
Diarrhoea			
subjects affected / exposed	1 / 310 (0.32%)	4 / 320 (1.25%)	2 / 308 (0.65%)
occurrences (all)	1	6	2
Constipation			

subjects affected / exposed	0 / 310 (0.00%)	1 / 320 (0.31%)	0 / 308 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	1 / 310 (0.32%)	0 / 320 (0.00%)	1 / 308 (0.32%)
occurrences (all)	1	0	1
Sensitive skin			
subjects affected / exposed	1 / 310 (0.32%)	0 / 320 (0.00%)	0 / 308 (0.00%)
occurrences (all)	1	0	0
Rash pruritic			
subjects affected / exposed	1 / 310 (0.32%)	0 / 320 (0.00%)	0 / 308 (0.00%)
occurrences (all)	1	0	0
Rash			
subjects affected / exposed	0 / 310 (0.00%)	0 / 320 (0.00%)	4 / 308 (1.30%)
occurrences (all)	0	0	4
Pruritus			
subjects affected / exposed	0 / 310 (0.00%)	1 / 320 (0.31%)	2 / 308 (0.65%)
occurrences (all)	0	1	2
Pityriasis rosea			
subjects affected / exposed	0 / 310 (0.00%)	0 / 320 (0.00%)	1 / 308 (0.32%)
occurrences (all)	0	0	1
Dermatitis contact			
subjects affected / exposed	0 / 310 (0.00%)	0 / 320 (0.00%)	1 / 308 (0.32%)
occurrences (all)	0	0	1
Dermatitis atopic			
subjects affected / exposed	0 / 310 (0.00%)	0 / 320 (0.00%)	1 / 308 (0.32%)
occurrences (all)	0	0	1
Cold sweat			
subjects affected / exposed	0 / 310 (0.00%)	1 / 320 (0.31%)	0 / 308 (0.00%)
occurrences (all)	0	1	0
Alopecia			
subjects affected / exposed	0 / 310 (0.00%)	1 / 320 (0.31%)	0 / 308 (0.00%)
occurrences (all)	0	1	0
Acne			
subjects affected / exposed	1 / 310 (0.32%)	2 / 320 (0.63%)	1 / 308 (0.32%)
occurrences (all)	1	2	1

Hirsutism			
subjects affected / exposed	1 / 310 (0.32%)	0 / 320 (0.00%)	0 / 308 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 310 (0.00%)	3 / 320 (0.94%)	0 / 308 (0.00%)
occurrences (all)	0	3	0
Micturition urgency			
subjects affected / exposed	0 / 310 (0.00%)	1 / 320 (0.31%)	0 / 308 (0.00%)
occurrences (all)	0	1	0
Endocrine disorders			
Polycystic ovarian syndrome			
subjects affected / exposed	0 / 310 (0.00%)	1 / 320 (0.31%)	1 / 308 (0.32%)
occurrences (all)	0	1	1
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	1 / 310 (0.32%)	2 / 320 (0.63%)	3 / 308 (0.97%)
occurrences (all)	1	2	3
Neck pain			
subjects affected / exposed	1 / 310 (0.32%)	0 / 320 (0.00%)	1 / 308 (0.32%)
occurrences (all)	1	0	1
Myalgia			
subjects affected / exposed	73 / 310 (23.55%)	88 / 320 (27.50%)	81 / 308 (26.30%)
occurrences (all)	86	116	112
Musculoskeletal pain			
subjects affected / exposed	0 / 310 (0.00%)	0 / 320 (0.00%)	1 / 308 (0.32%)
occurrences (all)	0	0	1
Medial tibial stress syndrome			
subjects affected / exposed	1 / 310 (0.32%)	0 / 320 (0.00%)	0 / 308 (0.00%)
occurrences (all)	1	0	0
Joint swelling			
subjects affected / exposed	0 / 310 (0.00%)	1 / 320 (0.31%)	1 / 308 (0.32%)
occurrences (all)	0	1	1
Joint range of motion decreased			
subjects affected / exposed	0 / 310 (0.00%)	0 / 320 (0.00%)	1 / 308 (0.32%)
occurrences (all)	0	0	1

Bone swelling			
subjects affected / exposed	1 / 310 (0.32%)	0 / 320 (0.00%)	0 / 308 (0.00%)
occurrences (all)	1	0	0
Back pain			
subjects affected / exposed	2 / 310 (0.65%)	2 / 320 (0.63%)	0 / 308 (0.00%)
occurrences (all)	2	2	0
Arthralgia			
subjects affected / exposed	53 / 310 (17.10%)	58 / 320 (18.13%)	46 / 308 (14.94%)
occurrences (all)	65	77	66
Tendon pain			
subjects affected / exposed	1 / 310 (0.32%)	0 / 320 (0.00%)	0 / 308 (0.00%)
occurrences (all)	1	0	0
Synovial cyst			
subjects affected / exposed	1 / 310 (0.32%)	0 / 320 (0.00%)	0 / 308 (0.00%)
occurrences (all)	1	0	0
Rotator cuff syndrome			
subjects affected / exposed	1 / 310 (0.32%)	0 / 320 (0.00%)	0 / 308 (0.00%)
occurrences (all)	1	0	0
Pain in jaw			
subjects affected / exposed	1 / 310 (0.32%)	0 / 320 (0.00%)	0 / 308 (0.00%)
occurrences (all)	1	0	0
Tendonitis			
subjects affected / exposed	0 / 310 (0.00%)	1 / 320 (0.31%)	1 / 308 (0.32%)
occurrences (all)	0	1	1
Infections and infestations			
Acute sinusitis			
subjects affected / exposed	0 / 310 (0.00%)	3 / 320 (0.94%)	3 / 308 (0.97%)
occurrences (all)	0	3	3
Bacterial vaginosis			
subjects affected / exposed	0 / 310 (0.00%)	0 / 320 (0.00%)	1 / 308 (0.32%)
occurrences (all)	0	0	1
Bacterial vulvovaginitis			
subjects affected / exposed	0 / 310 (0.00%)	0 / 320 (0.00%)	1 / 308 (0.32%)
occurrences (all)	0	0	1
Beta haemolytic streptococcal infection			

subjects affected / exposed	1 / 310 (0.32%)	0 / 320 (0.00%)	0 / 308 (0.00%)
occurrences (all)	1	0	0
Bronchitis			
subjects affected / exposed	0 / 310 (0.00%)	0 / 320 (0.00%)	1 / 308 (0.32%)
occurrences (all)	0	0	1
Bronchitis viral			
subjects affected / exposed	0 / 310 (0.00%)	1 / 320 (0.31%)	0 / 308 (0.00%)
occurrences (all)	0	1	0
COVID-19			
subjects affected / exposed	9 / 310 (2.90%)	9 / 320 (2.81%)	5 / 308 (1.62%)
occurrences (all)	9	9	5
Chlamydial infection			
subjects affected / exposed	1 / 310 (0.32%)	0 / 320 (0.00%)	1 / 308 (0.32%)
occurrences (all)	1	0	1
Conjunctivitis			
subjects affected / exposed	3 / 310 (0.97%)	0 / 320 (0.00%)	0 / 308 (0.00%)
occurrences (all)	3	0	0
Conjunctivitis bacterial			
subjects affected / exposed	1 / 310 (0.32%)	0 / 320 (0.00%)	0 / 308 (0.00%)
occurrences (all)	1	0	0
Eye infection			
subjects affected / exposed	0 / 310 (0.00%)	1 / 320 (0.31%)	0 / 308 (0.00%)
occurrences (all)	0	1	0
Fungal infection			
subjects affected / exposed	0 / 310 (0.00%)	0 / 320 (0.00%)	2 / 308 (0.65%)
occurrences (all)	0	0	2
Gastroenteritis			
subjects affected / exposed	1 / 310 (0.32%)	1 / 320 (0.31%)	2 / 308 (0.65%)
occurrences (all)	1	1	2
Gastroenteritis viral			
subjects affected / exposed	1 / 310 (0.32%)	1 / 320 (0.31%)	0 / 308 (0.00%)
occurrences (all)	1	1	0
Gonorrhoea			
subjects affected / exposed	1 / 310 (0.32%)	0 / 320 (0.00%)	0 / 308 (0.00%)
occurrences (all)	1	0	0
Hordeolum			

subjects affected / exposed	0 / 310 (0.00%)	0 / 320 (0.00%)	1 / 308 (0.32%)
occurrences (all)	0	0	1
Impetigo			
subjects affected / exposed	1 / 310 (0.32%)	0 / 320 (0.00%)	0 / 308 (0.00%)
occurrences (all)	1	0	0
Influenza			
subjects affected / exposed	4 / 310 (1.29%)	2 / 320 (0.63%)	10 / 308 (3.25%)
occurrences (all)	4	2	10
Nasopharyngitis			
subjects affected / exposed	11 / 310 (3.55%)	18 / 320 (5.63%)	4 / 308 (1.30%)
occurrences (all)	11	18	5
Otitis externa			
subjects affected / exposed	2 / 310 (0.65%)	0 / 320 (0.00%)	0 / 308 (0.00%)
occurrences (all)	2	0	0
Otitis media acute			
subjects affected / exposed	3 / 310 (0.97%)	1 / 320 (0.31%)	2 / 308 (0.65%)
occurrences (all)	3	1	3
Sinusitis bacterial			
subjects affected / exposed	0 / 310 (0.00%)	0 / 320 (0.00%)	1 / 308 (0.32%)
occurrences (all)	0	0	1
Rhinitis			
subjects affected / exposed	1 / 310 (0.32%)	1 / 320 (0.31%)	2 / 308 (0.65%)
occurrences (all)	1	1	3
Respiratory tract infection viral			
subjects affected / exposed	1 / 310 (0.32%)	1 / 320 (0.31%)	0 / 308 (0.00%)
occurrences (all)	1	1	0
Pyuria			
subjects affected / exposed	1 / 310 (0.32%)	0 / 320 (0.00%)	0 / 308 (0.00%)
occurrences (all)	1	0	0
Pilonidal disease			
subjects affected / exposed	1 / 310 (0.32%)	0 / 320 (0.00%)	0 / 308 (0.00%)
occurrences (all)	1	0	0
Pharyngotonsillitis			
subjects affected / exposed	0 / 310 (0.00%)	0 / 320 (0.00%)	1 / 308 (0.32%)
occurrences (all)	0	0	1
Pharyngitis streptococcal			

subjects affected / exposed	1 / 310 (0.32%)	2 / 320 (0.63%)	3 / 308 (0.97%)
occurrences (all)	1	2	3
Pharyngitis			
subjects affected / exposed	2 / 310 (0.65%)	4 / 320 (1.25%)	3 / 308 (0.97%)
occurrences (all)	2	4	3
Staphylococcal infection			
subjects affected / exposed	0 / 310 (0.00%)	0 / 320 (0.00%)	1 / 308 (0.32%)
occurrences (all)	0	0	1
Stitch abscess			
subjects affected / exposed	1 / 310 (0.32%)	0 / 320 (0.00%)	0 / 308 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract infection			
subjects affected / exposed	4 / 310 (1.29%)	10 / 320 (3.13%)	1 / 308 (0.32%)
occurrences (all)	5	10	1
Urethritis			
subjects affected / exposed	0 / 310 (0.00%)	0 / 320 (0.00%)	1 / 308 (0.32%)
occurrences (all)	0	0	1
Urinary tract infection			
subjects affected / exposed	0 / 310 (0.00%)	2 / 320 (0.63%)	1 / 308 (0.32%)
occurrences (all)	0	2	1
Viral infection			
subjects affected / exposed	3 / 310 (0.97%)	0 / 320 (0.00%)	3 / 308 (0.97%)
occurrences (all)	3	0	3
Viral pharyngitis			
subjects affected / exposed	0 / 310 (0.00%)	0 / 320 (0.00%)	1 / 308 (0.32%)
occurrences (all)	0	0	1
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 310 (0.32%)	1 / 320 (0.31%)	2 / 308 (0.65%)
occurrences (all)	1	1	2
Sinusitis			
subjects affected / exposed	1 / 310 (0.32%)	0 / 320 (0.00%)	2 / 308 (0.65%)
occurrences (all)	1	0	2
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 310 (0.00%)	1 / 320 (0.31%)	1 / 308 (0.32%)
occurrences (all)	0	1	1

Dehydration			
subjects affected / exposed	1 / 310 (0.32%)	0 / 320 (0.00%)	0 / 308 (0.00%)
occurrences (all)	1	0	0
Vitamin D deficiency			
subjects affected / exposed	2 / 310 (0.65%)	0 / 320 (0.00%)	0 / 308 (0.00%)
occurrences (all)	2	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 August 2019	As per the recommendation from CBER the study has been amended to include an update in development and validation of a new "agar-overlay" serum bactericidal assay using human serum complement (hSBA). Additional changes include validation of the MenB manual to measure immunogenicity of the meningococcal group B vaccine, a modification in the definition of 4-fold increase in post-vaccination hSBA titer definition when the pre-vaccination titer is below the limit of detection, and a modification in the population set to be used for safety analysis wherein the exposed set is to be used for all safety analyses.
23 January 2020	The inclusion of a booster recommendation in Menveo's US Prescription Insert, with the recommendation to administer the booster at least 4 years after the priming dose, has only been approved by US FDA in December 2019. As a result, the company intends to align the inclusion criterion in the V72_79 study with the recently introduced booster recommendation in the US and amend the protocol accordingly to allow inclusion of subjects who have received a meningococcal ACWY vaccine 4 years or greater in the past.
21 June 2022	The purpose of the amendment is to update the exclusion criteria of the protocol, align COVID-19 reporting requirements to local guidelines, and to update the definition of End of Study (EoS).
11 October 2022	The purpose of the amendment is to shorten the safety follow-up period to 6 months in subjects who have not reached the 6-month safety follow-up after the last dose and to extend the visit window to 28 days post reference day to mitigate the impact of COVID pandemic, including quarantine, mandatory vaccination, or other disturbances in the study procedures.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported