Clinical trial results:
A Phase 3b, Open Label, Controlled, Multi-Center, Extension Study to Assess the Persistence of Bactericidal Activity at 4 to 7.5 Years After Two Dose Primary Series of GlaxoSmithKline Biologicals Meningococcal B Recombinant Vaccine and the Response to a Third Dose in Adolescents and Young Adult Subjects who Previously Participated in Parent Studies V72_41 and V72P10, Compared to Naïve Healthy Controls

Summary

EudraCT number	2017-000093-11
Trial protocol	Outside EU/EEA
Global end of trial date	23 September 2016

Results information

Result version number	v2
This version publication date	30 November 2017
First version publication date	14 October 2017
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	205218

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02446743
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline Biologicals
Sponsor organisation address	Rue de l'Institut 89, Rixensart, Belgium, B-1330
Public contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 44 2089904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 44 2089904466, 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	22 June 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	22 September 2016
Global end of trial reached?	Yes
Global end of trial date	23 September 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

•To assess and compare the safety and tolerability of a single dose (booster) of rMenB+OMV NZ administered to follow-on subjects approximately 4 to 7.5 years after a 2 dose primary series, with that of two doses of rMenB+OMV NZ administered to naïve subjects according to a 0, 1-month schedule.
•To assess serum bactericidal activity at approximately 4 to 7.5 years following a 2 dose primary series (persistence) compared to serum bactericidal activity at baseline in vaccination-naïve subjects.

Protection of trial subjects:

The subjects were observed closely for at least 30 minutes following the administration of vaccine(s), with appropriate medical treatment readily available in case of a rare anaphylactic reaction.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 November 2015
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	Australia: 63
Country: Number of subjects enrolled	Canada: 187
Country: Number of subjects enrolled	Chile: 281
Worldwide total number of subjects	531
EEA total number of subjects	0

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)	122
Adults (18-64 years)	409

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were recruited from 4 sites in Australia, 6 sites in Canada and 2 sites in Chile.

Pre-assignment

Screening details:

All enrolled subjects were included in the study.

Period 1

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

Blinding implementation details:

The study was an open- label study. Therefore, no blinding procedures were utilized.

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 3B

Arm description:

Subjects who received a third dose booster of rMenB+OMV NZ at 4 to 7.5 years after the last dose received during studies V72P10 (NCT00661713) or V72_41(NCT0142384), and had blood collected at baseline and at 3, 7 and 30 days after the third dose booster.

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

Dosage and administration details:

One dose (0.5 mL) vaccine administered by intramuscular (IM) injection in the deltoid area of the nondominant arm

Arm title	Group B_0_1

Arm description:

Subjects who received two doses of rMenB+OMV NZ at a 0 and 1 month schedule and had blood collected at baseline, 30 days after the first dose and 3 or 7, and 30 days after the second dose.

Arm type	Active comparator
Investigational medicinal product name	GlaxoSmithKline Meningococcal group B multicomponent recombinant adsorbed vaccine
Investigational medicinal product code	
Other name	rMenB+OMV NZ
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

One dose (0.5 mL) vaccine administered by intramuscular (IM) injection in the deltoid area of the nondominant arm

Number of subjects in period 1	Group 3B	Group B_0_1
Started	276	255
Completed	271	250
Not completed	5	5
Consent withdrawn by subject	1	1
Adverse event, non-fatal	1	1
Unspecified	2	3
Lost to follow-up	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Group 3B
Reporting group description:	
Subjects who received a third dose booster of rMenB+OMV NZ at 4 to 7.5 years after the last dose received during studies V72P10 (NCT00661713) or V72_41(NCT0142384), and had blood collected at baseline and at 3, 7 and 30 days after the third dose booster.	
Reporting group title	Group B_0_1
Reporting group description:	
Subjects who received two doses of rMenB+OMV NZ at a 0 and 1 month schedule and had blood collected at baseline, 30 days after the first dose and 3 or 7, and 30 days after the second dose.	

Reporting group values	Group 3B	Group B_0_1	Total
Number of subjects	276	255	531
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)	65	57	122
Adults (18-64 years)	211	198	409
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	19.5	20.0	
standard deviation	± 2.42	± 2.69	-
Gender categorical			
Units: Subjects			
Female	133	128	261
Male	143	127	270
Race/Ethnicity, Customized			
Units: Subjects			
Race/Ethinicity American Indian or Alaska Native	11	1	12
Race/Ethinicity Asian	22	18	40
Race/Ethinicity Black or African American	3	2	5
Race/Ethinicity NativeHawaiian/pacific Islander	3	8	11
Race/Ethinicity White	98	74	172
Race/Ethinicity Other	139	152	291

End points

End points reporting groups

Reporting group title	Group 3B
Reporting group description:	
Subjects who received a third dose booster of rMenB+OMV NZ at 4 to 7.5 years after the last dose received during studies V72P10 (NCT00661713) or V72_41(NCT0142384), and had blood collected at baseline and at 3, 7 and 30 days after the third dose booster.	
Reporting group title	Group B_0_1
Reporting group description:	
Subjects who received two doses of rMenB+OMV NZ at a 0 and 1 month schedule and had blood collected at baseline, 30 days after the first dose and 3 or 7, and 30 days after the second dose.	

Primary: Percentage of subjects with human serum bactericidal activity (hSBA) ≥1:5

End point title	Percentage of subjects with human serum bactericidal activity (hSBA) ≥1:5
End point description:	
Bactericidal activity was measured against each of the N. meningitidis group B indicator strains H44/76, 5/99, NZ98/254 a nd M10713.	
End point type	Primary
End point timeframe:	
Group 3B: Day 1 (prior to booster dose); Group B_0_1: Day 1 (prior to first dose).	

End point values	Group 3B	Group B_0_1		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	275	255		
Units: Percentage of subjects				
number (confidence interval 95%)				
H44/76	33 (27.9 to 39.4)	9 (5.5 to 12.8)		
5/99	84 (78.7 to 88.2)	15 (10.4 to 19.8)		
NZ98/254	18 (13.3 to 22.6)	8 (5.2 to 12.4)		
M10713	74 (68.9 to 79.5)	70 (64.2 to 75.7)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description:	
The group difference in percentages of subjects with response against N. meningitidis group B indicator strain H44/76and the associated confidence interval for the difference was calculated using the method of Miettinen and Nurminen.	
Comparison groups	Group B_0_1 v Group 3B

Number of subjects included in analysis	530
Analysis specification	Pre-specified
Analysis type	other[1]
Method	Miettinen and Nurminen score method
Parameter estimate	vaccine group difference
Point estimate	25
Confidence interval	
level	95 %
sides	2-sided
lower limit	18.2
upper limit	31.4

Notes:

[1] - Vaccine comparison at Persistence at 4/7.5 years/Baseline in V72_75 (Group 3B vs. Group B_0_1)

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

The group difference in percentages of subjects with response against N. meningitidis group B indicator strain 5/99 and the associated confidence interval for the difference was calculated using the method of Miettinen and Nurminen.

Comparison groups	Group 3B v Group B_0_1
Number of subjects included in analysis	530
Analysis specification	Pre-specified
Analysis type	other[2]
Method	Miettinen and Nurminen score method
Parameter estimate	Vaccine group difference
Point estimate	69
Confidence interval	
level	95 %
sides	2-sided
lower limit	62.3
upper limit	75

Notes:

[2] - Vaccine comparison at Persistence at 4/7.5 years/Baseline in V72_75 (Group 3B vs. Group B_0_1)

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

The group difference in percentages of subjects with response against N. meningitidis group B indicator strain NZ98/254 and the associated confidence interval for the difference was calculated using the method of Miettinen and Nurminen.

Comparison groups	Group 3B v Group B_0_1
Number of subjects included in analysis	530
Analysis specification	Pre-specified
Analysis type	other[3]
Method	Miettinen and Nurminen score method
Parameter estimate	vaccine group difference
Point estimate	9
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.6
upper limit	15.1

Notes:

[3] - Vaccine comparison at Persistence at 4/7.5 years/Baseline in V72_75 (Group 3B vs. Group B_0_1)

Statistical analysis title	Statistical analysis 4

Statistical analysis description:

The group difference in percentages of subjects with response against N. meningitidis group B indicator strain M10713 and the associated confidence interval for the difference was calculated using the method of Miettinen and Nurminen.

Comparison groups	Group 3B v Group B_0_1
Number of subjects included in analysis	530
Analysis specification	Pre-specified
Analysis type	other[4]
Method	Miettinen and Nurminen score method
Parameter estimate	Vaccine group difference
Point estimate	4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.4
upper limit	11.9

Notes:

[4] - Vaccine comparison at Persistence at 4/7.5 years/Baseline in V72_75 (Group 3B vs. Group B_0_1)

Primary: Percentage of subjects with hSBA≥1:8

End point title	Percentage of subjects with hSBA≥1:8

End point description:

Bactericidal activity was measured against each of the N. meningitidis group B indicator strains H44/76,5/99,NZ98/254 and M10713

End point type	Primary

End point timeframe:

Group 3B: Day 1 (prior to booster dose); Group B_0_1: Day 1 (prior to first dose).

End point values	Group 3B	Group B_0_1		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	275	255		
Units: Percentage of subjects				
number (confidence interval 95%)				
H44/76	28 (23.1 to 34.1)	6 (3.3 to 9.5)		
5/99	81 (75.3 to 85.4)	13 (9.0 to 17.9)		
NZ98/254	14 (10.4 to 19.0)	6 (3.1 to 9.1)		
M10713	68 (62.0 to 73.4)	63 (56.9 to 69.1)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The group difference in percentages of subjects with response against N. meningitidis group B indicator strain H44/76 and the associated confidence interval for the difference was calculated using the method of Miettinen and Nurminen.

Comparison groups	Group 3B v Group B_0_1
Number of subjects included in analysis	530
Analysis specification	Pre-specified
Analysis type	other[5]
Method	Miettinen and Nurminen score method
Parameter estimate	Vaccine group difference
Point estimate	22
Confidence interval	
level	95 %
sides	2-sided
lower limit	16.5
upper limit	28.6

Notes:

[5] - Vaccine comparison at Persistence at 4/7.5 years/Baseline in V72_75 (Group 3B vs. Group B_0_1)

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

The group difference in percentages of subjects with response against N. meningitidis group B indicator strain 5/99 and the associated confidence interval for the difference was calculated using the method of Miettinen and Nurminen

Comparison groups	Group 3B v Group B_0_1
Number of subjects included in analysis	530
Analysis specification	Pre-specified
Analysis type	other[6]
Method	Miettinen and Nurminen score method
Parameter estimate	Vaccine group difference
Point estimate	68
Confidence interval	
level	95 %
sides	2-sided
lower limit	60.8
upper limit	73.7

Notes:

[6] - Vaccine comparison at Persistence at 4/7.5 years/Baseline in V72_75 (Group 3B vs. Group B_0_1)

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

The group difference in percentages of subjects with response against N. meningitidis group B indicator strain NZ98/254 and the associated confidence interval for the difference was calculated using the method of Miettinen and Nurminen

Comparison groups	Group 3B v Group B_0_1

Number of subjects included in analysis	530
Analysis specification	Pre-specified
Analysis type	other[7]
Method	Miettinen and Nurminen score method
Parameter estimate	Vaccine group difference
Point estimate	9
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.7
upper limit	14

Notes:

[7] - Vaccine comparison at Persistence at 4/7.5 years/Baseline in V72_75 (Group 3B vs. Group B_0_1)

Statistical analysis title	Statistical analysis 4

Statistical analysis description:

The group difference in percentages of subjects with response against N. meningitidis group B indicator strain M10713 and the associated confidence interval for the difference was calculated using the method of Miettinen and Nurminen

Comparison groups	Group 3B v Group B_0_1
Number of subjects included in analysis	530
Analysis specification	Pre-specified
Analysis type	other[8]
Method	Miettinen and Nurminen score method
Parameter estimate	Vaccine group difference
Point estimate	5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.4
upper limit	12.8

Notes:

[8] - Vaccine comparison at Persistence at 4/7.5 years/Baseline in V72_75 (Group 3B vs. Group B_0_1)

Primary: Percentage of subjects with hSBA≥1:16

End point title	Percentage of subjects with hSBA≥1:16

End point description:

Bactericidal activity was measured against each of the N. meningitidis group B Indicator strains H44/76,5/99,NZ98/254 and M10713

End point type	Primary

End point timeframe:

Group 3B: Day 1 (prior to booster dose); Group B_0_1: Day 1 (prior to first dose).

End point values	Group 3B	Group B_0_1		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	275	255		
Units: Percentage of subjects				
number (confidence interval 95%)				
H44/76	20 (15.1 to 24.8)	4 (2.2 to 7.6)		
5/99	75 (69.0 to 80.0)	8 (5.2 to 12.6)		
NZ98/254	11 (7.8 to 15.7)	2 (0.9 to 5.1)		
M10713	57 (51.2 to 63.2)	56 (49.4 to 61.9)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The group difference in percentages of subjects with response against N. meningitidis serogroup B indicator strain H44/76 and the associated confidence interval for the difference was calculated using the method of Miettinen and Nurminen

Comparison groups	Group 3B v Group B_0_1
Number of subjects included in analysis	530
Analysis specification	Pre-specified
Analysis type	other[9]
Method	Miettinen and Nurminen score method
Parameter estimate	Vaccine group difference
Point estimate	15
Confidence interval	
level	95 %
sides	2-sided
lower limit	10.1
upper limit	20.9

Notes:

[9] - Vaccine comparison at Persistence at 4/7.5 years/Baseline in V72_75 (Group 3B vs. Group B_0_1)

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

The group difference in percentages of subjects with response against N. meningitidis serogroup B indicator strain 5/99 and the associated confidence interval for the difference was calculated using the method of Miettinen and Nurminen

Comparison groups	Group 3B v Group B_0_1
Number of subjects included in analysis	530
Analysis specification	Pre-specified
Analysis type	other[10]
Method	Miettinen and Nurminen score method
Parameter estimate	vaccine group difference
Point estimate	66

Confidence interval	
level	95 %
sides	2-sided
lower limit	59.6
upper limit	72.4

Notes:

[10] - Vaccine comparison at Persistence at 4/7.5 years/Baseline in V72_75 (Group 3B vs. Group B_0_1)

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

The group difference in percentages of subjects with response against N. meningitidis serogroup B indicator strain NZ98/254 and the associated confidence interval for the difference was calculated using the method of Miettinen and Nurminen

Comparison groups	Group 3B v Group B_0_1
Number of subjects included in analysis	530
Analysis specification	Pre-specified
Analysis type	other[11]
Method	Miettinen and Nurminen score method
Parameter estimate	Vaccine group difference
Point estimate	9
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.9
upper limit	13.6

Notes:

[11] - Vaccine comparison at Persistence at 4/7.5 years/Baseline in V72_75 (Group 3B vs. Group B_0_1)

Statistical analysis title	Statistical analysis 4

Statistical analysis description:

The group difference in percentages of subjects with response against N. meningitidis serogroup B indicator strain M10713 and the associated confidence interval for the difference was calculated using the method of Miettinen and Nurminen

Comparison groups	Group 3B v Group B_0_1
Number of subjects included in analysis	530
Analysis specification	Pre-specified
Analysis type	other[12]
Method	Miettinen and Nurminen score method
Parameter estimate	Vaccine group difference
Point estimate	2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.8
upper limit	10

Notes:

[12] - Vaccine comparison at Persistence at 4/7.5 years/Baseline in V72_75 (Group 3B vs. Group B_0_1)

Primary: hSBA Geometric Mean Titers (GMTs) after the last dose of rMenB+OMV NZ vaccination in the parent study.

End point title	hSBA Geometric Mean Titers (GMTs) after the last dose of

	rMenB+OMV NZ vaccination in the parent study.

End point description:

Bactericidal activity was measured against each of the N. meningitidis group B indicator strains H44/76, 5/99, NZ98/254 a nd M10713.

End point type	Primary

End point timeframe:

Group 3B: 1 month after the last rMenB+OMV NZ vaccination in parent study and Day 1(prior to booster dose); Group B_0_1: Day 1(prior to first dose)

End point values	Group 3B	Group B_0_1		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	275	255		
Units: Titers				
geometric mean (confidence interval 95%)				
H44/76(1 month post last vacc in parent study)	124 (108 to 143)	0 (0 to 0)		
H44/76(Day 1)	3.05 (2.61 to 3.56)	1.20 (1.02 to 1.42)		
5/99(1 month post last vacc in parent study)	270 (234 to 311)	0 (0 to 0)		
5/99 (Day 1)	26 (21 to 31)	1.57 (1.26 to 1.95)		
NZ98/254(1 month post last vacc in parent study)	22 (19 to 27)	0 (0 to 0)		
NZ98/254(Day 1)	1.66 (1.46 to 1.89)	1.11 (0.97 to 1.27)		
M10713(1 month post last vacc in parent study)	19 (16 to 24)	0 (0 to 0)		
M10713(Day 1)	16 (13 to 20)	12 (9.86 to 16)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Adjusted geometric mean titers for H44/76 indicator strain were obtained by exponentiating (base 10) the least square means and the lower and upper limits of the 95% confidence intervals of the log-transformed titers obtained from an ANOVA estimation adjusting for vaccine group and country.

Comparison groups	Group B_0_1 v Group 3B
Number of subjects included in analysis	530
Analysis specification	Pre-specified
Analysis type	other[13]
Method	ANOVA
Parameter estimate	vaccine group ratio of GMTs
Point estimate	2.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.07
upper limit	3.12

Notes:

[13] - Vaccine Comparison at Persistence at 4 years/Baseline in V72_75 (Group 3B vs. Group B_0_1)

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

Adjusted geometric mean titers for 5/99 indicator strain were obtained by exponentiating (base 10) the least square means and the lower and upper limits of the 95% confidence intervals of the log-transformed titers obtained from an ANOVA estimation adjusting for vaccine group and country.

Comparison groups	Group B_0_1 v Group 3B
Number of subjects included in analysis	530
Analysis specification	Pre-specified
Analysis type	other[14]
Method	ANOVA
Parameter estimate	Vaccine group ratio of GMTs
Point estimate	16
Confidence interval	
level	95 %
sides	2-sided
lower limit	12
upper limit	21

Notes:

[14] - Vaccine Comparison at Persistence at 4 years/Baseline in V72_75 (Group 3B vs. Group B_0_1)

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

Adjusted geometric mean titers for NZ98/254 indicator strain were obtained by exponentiating (base 10) the least square means and the lower and upper limits of the 95% confidence intervals of the log-transformed titers obtained from an ANOVA estimation adjusting for vaccine group and country

Comparison groups	Group B_0_1 v Group 3B
Number of subjects included in analysis	530
Analysis specification	Pre-specified
Analysis type	other[15]
Method	ANOVA
Parameter estimate	Vaccine group ratio of GMTs
Point estimate	1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.26
upper limit	1.78

Notes:

[15] - Vaccine Comparison at Persistence at 4 years/Baseline in V72_75 (Group 3B vs. Group B_0_1)

Statistical analysis title	Statistical analysis 4

Statistical analysis description:

Adjusted geometric mean titers for M10713 indicator strain were obtained by exponentiating (base 10) the least square means and the lower and upper limits of the 95% confidence intervals of the log-transformed titers obtained from an ANOVA estimation adjusting for vaccine group and country

Comparison groups	Group B_0_1 v Group 3B

Number of subjects included in analysis	530
Analysis specification	Pre-specified
Analysis type	other[16]
Method	ANOVA
Parameter estimate	Vaccine group ratio of GMTs
Point estimate	1.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.94
upper limit	1.68

Notes:

[16] - Vaccine Comparison at Persistence at 4 years/Baseline in V72_75 (Group 3B vs. Group B_0_1)

Primary: Geometric Mean Ratios (GMRs) of GMTs after the last dose of rMenB+OMV NZ Vaccination in the Parent Study.

End point title	Geometric Mean Ratios (GMRs) of GMTs after the last dose of rMenB+OMV NZ Vaccination in the Parent Study.[17][18]

End point description:

The GMRs of GMTs at Day 1 versus one month after the last dose of rMenB+OMV NZ vaccination in the parent study were calculated. Bactericidal activity was measured against each of the N. meningitidis group B indicator strains H44/76,5/99,NZ98/254 and M10713.

End point type	Primary

End point timeframe:

Group 3B: 1 month after the last vaccination in parent study and Day1 (prior to booster dose)

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 scope of this primary end point was descriptive, no statistical hypothesis test was performed.
[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

End point values	Group 3B			
Subject group type	Reporting group			
Number of subjects analysed	275			
Units: Ratio				
geometric mean (confidence interval 95%)				
H44/76	0.025 (0.020 to 0.030)			
5/99	0.098 (0.079 to 0.12)			
NZ98/254	0.073 (0.059 to 0.089)			
M10713	0.81 (0.65 to 1.01)			

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with solicited local and systemic AEs.

End point title	Number of subjects with solicited local and systemic AEs.[19]

End point description:

Solicited adverse events are signs and symptoms derived from organized data collection systems, such as Subject Diaries or interview. The percentage and frequencies of subjects reporting solicited local and systemic AEs were tabulated. Threshold for any Erythema, Swelling and Induration: >= 25 mm
Note:Vaccination 2 was performed only on group B_0_1 subjects.

End point type	Primary

End point timeframe:

7 days (including the day of vaccination) after each vaccination

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 scope of this primary end point was descriptive, no statistical hypothesis test was performed.

End point values	Group 3B	Group B_0_1		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	266	254		
Units: Subjects				
Any	263	251		
Any Local (vaccination 1)	258	247		
Injection site pain (vaccination 1)	258	247		
Erythema (vaccination 1)	54	18		
Swelling (vaccination 1)	60	34		
Induration (vaccination 1)	54	26		
Any systemic (vaccination 1)	203	163		
Fever (≥ 38.0°C) (vaccination 1)	16	4		
High fever (≥ 39.5°C) (vaccination 1)	0	0		
Nausea (vaccination 1)	56	30		
Fatigue (vaccination 1)	155	110		
Myalgia (vaccination 1)	120	71		
Arthralgia (vaccination 1)	84	47		
Headache (vaccination 1)	146	94		
Any Local (vaccination 2)	0	226		
Injection site pain (vaccination 2)	0	226		
Erythema (vaccination 2)	0	21		
Swelling (vaccination 2)	0	32		
Induration (vaccination 2)	0	31		
Any systemic (vaccination 2)	0	140		
Fever (≥ 38.0°C) (vaccination 2)	0	5		
High fever (≥ 39.5°C) (vaccination 2)	0	0		
Nausea (vaccination 2)	0	33		
Fatigue (vaccination 2)	0	92		
Myalgia (vaccination 2)	0	64		
Arthralgia (vaccination 2)	0	36		
Headache (vaccination 2)	0	84		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with any unsolicited adverse events (AEs).

End point title	Number of subjects with any unsolicited adverse events

End point description:

An unsolicited adverse event is an adverse event that was not solicited using a Subject Diary and that was spontaneously communicated by a subject and/or parent(s)/legal guardian(s) who has signed the informed consent. Note : Vaccination 2 was performed only on group B_0_1 subjects.

End point type	Primary

End point timeframe:

30 days (including the day of vaccination) after each vaccination.

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 scope of this primary end point was descriptive, no statistical hypothesis test was performed.

End point values	Group 3B	Group B_0_1		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	275	255		
Units: Subjects				
Any	87	131		
Any unsolicited AEs (vaccination 1)	87	96		
Any unsolicited AEs (vaccination 2)	0	73		

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of subjects with any SAEs, AEs leading to withdrawal and medically attended AEs.[21]

End point description:

A serious adverse event is any untoward medical occurrence that at any dose results in death or is life threatening or requires prolonged hospitalization, leads to Persistent or significant disability/incapacity.

End point type	Primary

End point timeframe:

Group 3B: from Day 1 to Day 31 (30 days after the vaccination) and Group B_0_1: from Day 1 to Day 61 (30 days after the second dose)

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 scope of this primary end point was descriptive, no statistical hypothesis test was performed.

End point values	Group 3B	Group B_0_1		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	275	255		
Units: Subjects				
Any SAEs	0	1		
Any Medically Attended AEs	17	34		
Any AEs leading to premature withdrawal	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with hSBA ≥1:5 after booster dose/first vaccination of rMenB+OMV NZ.

End point title	Percentage of subjects with hSBA ≥1:5 after booster dose/first vaccination of rMenB+OMV NZ.

End point description:

Bactericidal activity was measured against each of the four N. meningitidis group B indicator strains H44/76,5/99,NZ98/254 and M10713.

End point type	Secondary

End point timeframe:

Group 3B: 1 month after booster dose, Group B_0_1 : 30 days after first vaccination.

End point values	Group 3B	Group B_0_1		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	268	253		
Units: Percentage of subjects				
number (confidence interval 95%)				
H44/76	99 (96.8 to 99.77)	79 (73.5 to 83.9)		
5/99	100 (98.4 to 100.0)	84 (78.9 to 88.6)		
NZ98/254	93 (88.9 to 95.6)	52 (45.4 to 58.1)		
M10713	99 (96.8 to 99.77)	87 (82.1 to 90.8)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The group difference in percentages of subjects with response against N. meningitidis serogroup B indicator strain H44/76 and the associated confidence interval for the difference were calculated using the method of Miettinen and Nurminen

Comparison groups	Group 3B v Group B_0_1

Number of subjects included in analysis	521
Analysis specification	Pre-specified
Analysis type	other[22]
Method	Miettinen and Nurminen score method
Parameter estimate	Vaccine group difference
Point estimate	20
Confidence interval	
level	95 %
sides	2-sided
lower limit	15
upper limit	25.4

Notes:

[22] - Vaccine comparison at 1 month after booster /1st dose in V72_75 (Group 3B vs. Group B_0_1)

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

The group difference in percentages of subjects with response against N. meningitidis serogroup B indicator strain 5/99 and the associated confidence interval for the difference were calculated using the method of Miettinen and Nurminen

Comparison groups	Group 3B v Group B_0_1
Number of subjects included in analysis	521
Analysis specification	Pre-specified
Analysis type	other[23]
Method	Miettinen and Nurminen score method
Parameter estimate	vaccine group difference
Point estimate	16
Confidence interval	
level	95 %
sides	2-sided
lower limit	11.7
upper limit	21

Notes:

[23] - Vaccine comparison at 1 month after booster /1st dose in V72_75 (Group 3B vs. Group B_0_1)

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

The group difference in percentages of subjects with response against N. meningitidis serogroup B indicator strain NZ98/254 and the associated confidence interval for the difference were calculated using the method of Miettinen and Nurminen.

Comparison groups	Group 3B v Group B_0_1
Number of subjects included in analysis	521
Analysis specification	Pre-specified
Analysis type	other[24]
Method	Miettinen and Nurminen score method
Parameter estimate	vaccine group difference
Point estimate	41
Confidence interval	
level	95 %
sides	2-sided
lower limit	33.9
upper limit	47.8

Notes:

[24] - Vaccine comparison at 1 month after booster /1st dose in V72_75 (Group 3B vs. Group B_0_1)

Statistical analysis title	Statistical analysis 4

Statistical analysis description:

The group difference in percentages of subjects with response against N. meningitidis serogroup B indicator strain M10713 and the associated confidence interval for the difference was calculated using the method of Miettinen and Nurminen

Comparison groups	Group 3B v Group B_0_1
Number of subjects included in analysis	521
Analysis specification	Pre-specified
Analysis type	other[25]
Method	Miettinen and Nurminen score method
Parameter estimate	vaccine group difference
Point estimate	12
Confidence interval	
level	95 %
sides	2-sided
lower limit	8
upper limit	16.8

Notes:

[25] - Vaccine comparison at 1 month after booster /1st dose in V72_75 (Group 3B vs. Group B_0_1)

Secondary: Percentage of subjects with hSBA ≥1:8 after booster dose/first vaccination of rMenB+OMV NZ

End point title	Percentage of subjects with hSBA ≥1:8 after booster dose/first vaccination of rMenB+OMV NZ

End point description:

Bactericidal activity was measured against each of the four N. meningitidis group B indicator strains H44/76,5/99,NZ98/254 and M10713.

End point type	Secondary

End point timeframe:

Group 3B : 1 month after booster dose, Group B_0_1 : 30 days after first vaccination.

End point values	Group 3B	Group B_0_1		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	268	253		
Units: Percentage of subjects				
number (confidence interval 95%)				
H44/76	99 (96.8 to 99.77)	72 (65.6 to 77.0)		
5/99	100 (98.4 to 100.0)	81 (75.6 to 86.0)		
NZ98/254	87 (82.8 to 91.2)	45 (38.4 to 51.0)		
M10713	98 (95.7 to 99.4)	85 (79.9 to 89.1)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The group difference in percentages of subjects with response against N. meningitidis serogroup B indicator strain H44/76 and the associated confidence interval for the difference were calculated using the method of Miettinen and Nurminen

Comparison groups	Group B_0_1 v Group 3B
Number of subjects included in analysis	521
Analysis specification	Pre-specified
Analysis type	other[26]
Method	Miettinen and Nurminen score method
Parameter estimate	Vaccine group difference
Point estimate	27
Confidence interval	
level	95 %
sides	2-sided
lower limit	21.9
upper limit	33.3

Notes:

[26] - Vaccine comparison at 1 month after booster /1st dose in V72_75 (Group 3B vs. Group B_0_1)

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

The group difference in percentages of subjects with response against N. meningitidis serogroup B indicator strain 5/99 and the associated confidence interval for the difference were calculated using the method of Miettinen and Nurminen

Comparison groups	Group B_0_1 v Group 3B
Number of subjects included in analysis	521
Analysis specification	Pre-specified
Analysis type	other[27]
Method	Miettinen and Nurminen score method
Parameter estimate	vaccine group difference
Point estimate	19
Confidence interval	
level	95 %
sides	2-sided
lower limit	14.3
upper limit	24.3

Notes:

[27] - Vaccine comparison at 1 month after booster /1st dose in V72_75 (Group 3B vs. Group B_0_1)

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

The group difference in percentages of subjects with response against N. meningitidis serogroup B

indicator strain NZ98/254 and the associated confidence interval for the difference were calculated using the method of Miettinen and Nurminen

Comparison groups	Group B_0_1 v Group 3B
Number of subjects included in analysis	521
Analysis specification	Pre-specified
Analysis type	other[28]
Method	Miettinen and Nurminen score method
Parameter estimate	vaccine group difference
Point estimate	43
Confidence interval	
level	95 %
sides	2-sided
lower limit	35.2
upper limit	49.9

Notes:

[28] - Vaccine comparison at 1 month after booster /1st dose in V72_75 (Group 3B vs. Group B_0_1)

Statistical analysis title	Statistical analysis 4

Statistical analysis description:

The group difference in percentages of subjects with response against N. meningitidis serogroup B indicator strain M10713 and the associated confidence interval for the difference were calculated using the method of Miettinen and Nurminen.

Comparison groups	Group B_0_1 v Group 3B
Number of subjects included in analysis	521
Analysis specification	Pre-specified
Analysis type	other[29]
Method	Miettinen and Nurminen score method
Parameter estimate	vaccine group difference
Point estimate	13
Confidence interval	
level	95 %
sides	2-sided
lower limit	8.8
upper limit	18.3

Notes:

[29] - Vaccine comparison at 1 month after booster /1st dose in V72_75 (Group 3B vs. Group B_0_1)

Secondary: Percentage of subjects with hSBA ≥1:16 after booster dose/first vaccination of rMenB+OMV NZ

End point title	Percentage of subjects with hSBA ≥1:16 after booster dose/first vaccination of rMenB+OMV NZ

End point description:

Bactericidal activity was measured against each of the four N. meningitidis group B indicator strains.

End point type	Secondary

End point timeframe:

Group 3B: 1 month after booster dose, Group B_0_1 : 30 days after first vaccination.

End point values	Group 3B	Group B_0_1		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	268	253		
Units: Percentage of subjects				
number (confidence interval 95%)				
H44/76	99 (96.2 to 99.59)	58 (52.2 to 64.6)		
5/99	100 (98.4 to 100.0)	73 (66.9 to 78.6)		
NZ98/254	79 (73.6 to 83.8)	36 (29.9 to 42.1)		
M10713	95 (91.8 to 97.4)	77 (70.9 to 81.7)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The group difference in percentages of subjects with response against N. meningitidis serogroup B indicator strain H44/76 and the associated confidence interval for the difference was calculated using the method of Miettinen and Nurminen

Comparison groups	Group B_0_1 v Group 3B
Number of subjects included in analysis	521
Analysis specification	Pre-specified
Analysis type	other[30]
Method	Miettinen and Nurminen score method
Parameter estimate	vaccine group difference
Point estimate	40
Confidence interval	
level	95 %
sides	2-sided
lower limit	33.9
upper limit	46.3

Notes:

[30] - Vaccine comparison at 1 month after booster /1st dose in V72_75 (Group 3B vs. Group B_0_1)

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

The group difference in percentages of subjects with response against N. meningitidis serogroup B indicator strain 5/99 and the associated confidence interval for the difference was calculated using the method of Miettinen and Nurminen

Comparison groups	Group B_0_1 v Group 3B
Number of subjects included in analysis	521
Analysis specification	Pre-specified
Analysis type	other[31]
Method	Miettinen and Nurminen score method
Parameter estimate	vaccine group difference
Point estimate	27

Confidence interval	
level	95 %
sides	2-sided
lower limit	21.6
upper limit	33

Notes:

[31] - Vaccine comparison at 1 month after booster /1st dose in V72_75 (Group 3B vs. Group B_0_1)

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

The group difference in percentages of subjects with response against N. meningitidis serogroup B indicator strain NZ98/254 and the associated confidence interval for the difference was calculated using the method of Miettinen and Nurminen

Comparison groups	Group B_0_1 v Group 3B
Number of subjects included in analysis	521
Analysis specification	Pre-specified
Analysis type	other[32]
Method	Miettinen and Nurminen score method
Parameter estimate	vaccine group difference
Point estimate	43
Confidence interval	
level	95 %
sides	2-sided
lower limit	35.1
upper limit	50.6

Notes:

[32] - Vaccine comparison at 1 month after booster /1st dose in V72_75 (Group 3B vs. Group B_0_1)

Statistical analysis title	Statistical analysis 4

Statistical analysis description:

The group difference in percentages of subjects with response against N. meningitidis serogroup B indicator strain M10713 and the associated confidence interval for the difference was calculated using the method of Miettinen and Nurminen

Comparison groups	Group B_0_1 v Group 3B
Number of subjects included in analysis	521
Analysis specification	Pre-specified
Analysis type	other[33]
Method	Miettinen and Nurminen score method
Parameter estimate	vaccine group difference
Point estimate	19
Confidence interval	
level	95 %
sides	2-sided
lower limit	12.9
upper limit	24.6

Notes:

[33] - Vaccine comparison at 1 month after booster /1st dose in V72_75 (Group 3B vs. Group B_0_1)

Secondary: hSBA Geometric Mean Titers prior to booster/first dose of vaccination & post booster/first dose of vaccination.

End point title	hSBA Geometric Mean Titers prior to booster/first dose of

	vaccination & post booster/first dose of vaccination.

End point description:

Bactericidal activity was measured against each of the four N. meningitidis group B indicator strains H44/76, 5/99,NZ98/254 and M10713

End point type	Secondary

End point timeframe:

Group 3B subjects: Day 1(pre-booster dose) and 1 month post-booster dose. Group B_0_1: Day 1 (pre-first dose) and 30 days post-first dose.

End point values	Group 3B	Group B_0_1		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	268	253		
Units: Titers				
geometric mean (confidence interval 95%)				
H44/76- pre booster/ pre first dose	3.10 (2.65 to 3.62)	1.19 (1.01 to 1.41)		
H44/76-1 month post booster/first dose	188 (155 to 228)	16 (13 to 20)		
5/99- pre booster/ pre first dose	24 (19 to 30)	1.51 (1.21 to 1.88)		
5/99-1 month post booster/first dose	2089 (1690 to 2582)	31 (25 to 38)		
NZ98/254-pre booster/ pre first dose	1.64 (1.44 to 1.86)	1.11 (0.97 to 1.28)		
NZ98/254-1 month post booster/first dose	32 (26 to 39)	5.39 (4.33 to 6.72)		
M10713-pre booster/ pre first dose	16 (13 to 20)	12 (9.62 to 15)		
M10713-1 month post booster/first dose	78 (66 to 92)	30 (25 to 36)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Pre booster/Pre first dose-Adjusted geometric mean titers for H44/76 indicator strain were obtained by exponentiating (base 10) the least square means and the lower and upper limits of the 95% confidence intervals of the log-transformed titers obtained from an ANOVA estimation adjusting for vaccine group and country.

Comparison groups	Group 3B v Group B_0_1
Number of subjects included in analysis	521
Analysis specification	Pre-specified
Analysis type	other[34]
Method	ANOVA
Parameter estimate	Vaccine group ratios
Point estimate	2.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.11
upper limit	3.2

Notes:

[34] - Vaccine comparison Pre-booster or pre-1st dose in V72_75 (Group 3B vs. Group B _0_1)

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

Post booster/Post first dose-Adjusted geometric mean titers for H44/76 indicator strain were obtained by exponentiating (base 10) the least square means and the lower and upper limits of the 95% confidence intervals of the log-transformed titers obtained from an ANOVA estimation adjusting for vaccine group and country

Comparison groups	Group 3B v Group B_0_1
Number of subjects included in analysis	521
Analysis specification	Pre-specified
Analysis type	other[35]
Method	ANOVA
Parameter estimate	vaccine group ratios
Point estimate	11
Confidence interval	
level	95 %
sides	2-sided
lower limit	8.85
upper limit	15

Notes:

[35] - Vaccine comparison Pre-booster or pre-1st dose in V72_75 (Group 3B vs. Group B _0_1)

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

Pre booster/Pre first dose-Adjusted geometric mean titers for 5/99 indicator strain were obtained by exponentiating (base 10) the least square means and the lower and upper limits of the 95% confidence intervals of the log-transformed titers obtained from an ANOVA estimation adjusting for vaccine group and country

Comparison groups	Group 3B v Group B_0_1
Number of subjects included in analysis	521
Analysis specification	Pre-specified
Analysis type	other[36]
Method	ANOVA
Parameter estimate	vaccine group ratios
Point estimate	16
Confidence interval	
level	95 %
sides	2-sided
lower limit	12
upper limit	21

Notes:

[36] - Vaccine comparison Pre-booster or pre-1st dose in V72_75 (Group 3B vs. Group B _0_1)

Statistical analysis title	Statistical analysis 4

Statistical analysis description:

Post booster/Post first dose-Adjusted geometric mean titers for 5/99 indicator strain were obtained by exponentiating (base 10) the least square means and the lower and upper limits of the 95% confidence intervals of the log-transformed titers obtained from an ANOVA estimation adjusting for vaccine group and country

Comparison groups	Group 3B v Group B_0_1

Number of subjects included in analysis	521
Analysis specification	Pre-specified
Analysis type	other[37]
Method	ANOVA
Parameter estimate	Vaccine group ratios
Point estimate	68
Confidence interval	
level	95 %
sides	2-sided
lower limit	51
upper limit	90

Notes:

[37] - Vaccine comparison Pre-booster or pre-1st dose in V72_75 (Group 3B vs. Group B _0_1)

Statistical analysis title	Statistical analysis 5

Statistical analysis description:

Pre booster/Pre first dose-Adjusted geometric mean titers for NZ98/254 indicator strain were obtained by exponentiating (base 10) the least square means and the lower and upper limits of the 95% confidence intervals of the log-transformed titers obtained from an ANOVA estimation adjusting for vaccine group and country

Comparison groups	Group 3B v Group B_0_1
Number of subjects included in analysis	521
Analysis specification	Pre-specified
Analysis type	other[38]
Method	ANOVA
Parameter estimate	Vaccine group ratios
Point estimate	1.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.24
upper limit	1.75

Notes:

[38] - Vaccine comparison Pre-booster or pre-1st dose in V72_75 (Group 3B vs. Group B _0_1)

Statistical analysis title	Statistical analysis 6

Statistical analysis description:

post booster dose/ first dose-Adjusted geometric mean titers for NZ98/254 indicator strain were obtained by exponentiating (base 10) the least square means and the lower and upper limits of the 95% confidence intervals of the log-transformed titers obtained from an ANOVA estimation adjusting for vaccine group and country.

Comparison groups	Group 3B v Group B_0_1
Number of subjects included in analysis	521
Analysis specification	Pre-specified
Analysis type	other[39]
Method	ANOVA
Parameter estimate	vaccine group ratios
Point estimate	5.9

Confidence interval	
level	95 %
sides	2-sided
lower limit	4.49
upper limit	7.76

Notes:

[39] - Vaccine comparison Pre-booster or pre-1st dose in V72_75 (Group 3B vs. Group B _0_1)

Statistical analysis title	Statistical analysis 7

Statistical analysis description:

Pre booster/Pre first dose-Adjusted geometric mean titers for M10713 indicator strain were obtained by exponentiating (base 10) the least square means and the lower and upper limits of the 95% confidence intervals of the log-transformed titers obtained from an ANOVA estimation adjusting for vaccine group and country

Comparison groups	Group 3B v Group B_0_1
Number of subjects included in analysis	521
Analysis specification	Pre-specified
Analysis type	other[40]
Method	ANOVA
Parameter estimate	vaccine group ratios
Point estimate	1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.97
upper limit	1.75

Notes:

[40] - Vaccine comparison Pre-booster or pre-1st dose in V72_75 (Group 3B vs. Group B _0_1)

Statistical analysis title	Statistical analysis 8

Statistical analysis description:

Post booster/Post first dose-Adjusted geometric mean titers for M10713 indicator strain were obtained by exponentiating (base 10) the least square means and the lower and upper limits of the 95% confidence intervals of the log-transformed titers obtained from an ANOVA estimation adjusting for vaccine group and country

Comparison groups	Group 3B v Group B_0_1
Number of subjects included in analysis	521
Analysis specification	Pre-specified
Analysis type	other[41]
Method	ANOVA
Parameter estimate	vaccine group ratios
Point estimate	2.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.08
upper limit	3.25

Notes:

[41] - Vaccine comparison Pre-booster or pre-1st dose in V72_75 (Group 3B vs. Group B _0_1)

Secondary: Geometric mean ratio (GMRs) of GMTs after booster dose/first rMenB+OMV NZ vaccination.

End point title	Geometric mean ratio (GMRs) of GMTs after booster dose/first rMenB+OMV NZ vaccination.

End point description:

Bactericidal activity was measured against each of the fout N. meningitidis group B indicator strains H44/76,5/99,NZ98/254 and M10713 by calculating the GMRs of GMTs one month post-vaccination of a booster dose versus pre-booster dose (follow-on subjects) or first dose of rMenB+OMV NZ versus pre-first dose (naïve subjects) to each N. meningitidis group B indicator strain.

End point type	Secondary

End point timeframe:

At Day 31 (30 days post booster dose/first dose of vaccination) versus Day 1 (prior to booster dose/first dose of vaccination).

End point values	Group 3B	Group B_0_1		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	268	253		
Units: Ratio				
geometric mean (confidence interval 95%)				
H44/76	61 (50 to 74)	14 (11 to 17)		
5/99	87 (67 to 112)	20 (16 to 26)		
NZ98/254	19 (16 to 24)	4.92 (3.97 to 6.10)		
M10713	4.85 (4.10 to 5.72)	2.44 (2.04 to 2.91)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentages of subjects with at least 4-fold increase in hSBA titers pre vaccination compared to one month post-booster/first rMenB+OMV NZ vaccination

End point title	Percentages of subjects with at least 4-fold increase in hSBA titers pre vaccination compared to one month post-booster/first rMenB+OMV NZ vaccination

End point description:

The percentage of subjects with 4-fold rise at one month post-vaccination with a booster dose (follow-on subjects) /first dose (naive subjects) of rMenB+OMV NZ with respect to day 1 (follow-on subjects) / pre-first dose of rMenB+OMV NZ (naïve subjects)

End point type	Secondary

End point timeframe:

Group 3B: 1 month after booster dose; Group B_0_1: 1 month after first vaccination

End point values	Group 3B	Group B_0_1		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	268	253		
Units: Percentage of subjects				
number (confidence interval 95%)				
H44/76	96 (93.2 to 98.2)	70 (63.5 to 75.2)		
5/99	98 (94.6 to 99.2)	76 (69.9 to 81.4)		
NZ98/254	80 (75.0 to 85.0)	43 (36.3 to 49.0)		
M10713	49 (42.6 to 54.9)	26 (20.5 to 31.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with hSBA ≥1:5 after booster dose/second vaccination of rMenB+OMV NZ

End point title	Percentage of subjects with hSBA ≥1:5 after booster dose/second vaccination of rMenB+OMV NZ

End point description:

Bactericidal activity was measured against each of the four N. meningitidis group B indicator strains H44/76,5/99,NZ98/254 and M10713. On day 1, subjects in the Group B_0_1 were to be randomized into 2 different blood draw schedules according to a 1:1 ratio : 2 blood samples at different time points: Group B_0_1_1: blood draws at 3 and 30 days after the second dose. Group B_0_1_2: blood draws at 7 and 30 days after the second dose.

End point type	Secondary

End point timeframe:

Group 3B: 3, 7 and 30 days after third dose booster; Group B_0_1: At 3 (group B_0_1_1 only), 7 (sub-group B_0_1_2 only) and 30 days post-second dose."

End point values	Group 3B	Group B_0_1		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	242	203		
Units: Percentage of subjects				
number (confidence interval 95%)				
H44/76 3 days post vaccination	36 (30.3 to 42.8)	80 (71.1 to 87.2)		
H44/76 7 days post vaccination	98 (95.2 to 99.3)	99 (94.4 to 99.97)		
H44/76 1 month post vaccination	99 (96.4 to 99.74)	99 (96.5 to 99.88)		
5/99- 3 days post-vaccination	78 (71.7 to 84.1)	83 (72.9 to 89.9)		
5/99- 7 days post-vaccination	100 (98.0 to 100.0)	99 (93.8 to 99.97)		
5/99- 1 month post-vaccination	100 (98.0 to 100.0)	99 (95.9 to 99.86)		

NZ98/254- 3 days post-vaccination	18 (12.9 to 23.1)	44 (34.1 to 53.8)		
NZ98/254- 7 days post-vaccination	74 (67.7 to 79.3)	79 (69.1 to 86.2)		
NZ98/254- 1 month post-vaccination	93 (88.6 to 95.7)	76 (69.9 to 82.0)		
M10713- 3 days post-vaccination	78 (72.2 to 83.1)	82 (73.2 to 88.7)		
M10713- 7 days post-vaccination	98 (94.7 to 99.1)	96 (89.9 to 98.9)		
M10713- 1 month post-vaccination	99 (97.0 to 99.90)	93 (88.7 to 96.2)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

3 days post vaccination-The group difference in percentages of subjects with response against N. meningitidis serogroup B indicator strain H44/76 and the associated confidence interval for the difference was calculated using the method of Miettinen and Nurminen.

Comparison groups	Group 3B v Group B_0_1
Number of subjects included in analysis	445
Analysis specification	Pre-specified
Analysis type	other[42]
Method	Miettinen and Nurminen score method
Parameter estimate	vaccine group difference
Point estimate	-44
Confidence interval	
level	95 %
sides	2-sided
lower limit	-52.7
upper limit	-33.1

Notes:

[42] - Vaccine comparison at Day 4 Group 3B vs Day 34 Group B_0_1 (3 days after booster or 2nd dose)

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

7 days post vaccination-The group difference in percentages of subjects with response against N. meningitidis serogroup B indicator strain H44/76 and the associated confidence interval for the difference was calculated using the method of Miettinen and Nurminen

Comparison groups	Group 3B v Group B_0_1
Number of subjects included in analysis	445
Analysis specification	Pre-specified
Analysis type	other[43]
Method	Miettinen and Nurminen score method
Parameter estimate	vaccine group difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.9
upper limit	3.6

Notes:

[43] - Vaccine comparison at Day 8 Group 3B vs Day 38 Group B_0_1 (7 days after booster or 2nd dose)

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

1 month post vaccination-The group difference in percentages of subjects with response against N. meningitidis serogroup B indicator strain H44/76 and the associated confidence interval for the difference was calculated using the method of Miettinen and Nurminen

Comparison groups	Group 3B v Group B_0_1
Number of subjects included in analysis	445
Analysis specification	Pre-specified
Analysis type	other[44]
Method	Miettinen and Nurminen score method
Parameter estimate	vaccine group difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.7
upper limit	2.4

Notes:

[44] - Vaccine comparison at Day 31 Group 3B vs Day 61 Group B_0_1 (1 month after booster or 2nd dose)

Statistical analysis title	Statistical analysis 4

Statistical analysis description:

3 days post vaccination-The group difference in percentages of subjects with response against N. meningitidis serogroup B indicator strain 5/99 and the associated confidence interval for the difference was calculated using the method of Miettinen and Nurminen

Comparison groups	Group 3B v Group B_0_1
Number of subjects included in analysis	445
Analysis specification	Pre-specified
Analysis type	other[45]
Method	Miettinen and Nurminen score method
Parameter estimate	vaccine group difference
Point estimate	-4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.6
upper limit	6.6

Notes:

[45] - Vaccine comparison at Day 4 Group 3B vs Day 34 Group B_0_1 (3 days after booster or 2nd dose)

Statistical analysis title	Statistical analysis 5

Statistical analysis description:

7 days post vaccination-The group difference in percentages of subjects with response against N. meningitidis serogroup B indicator strain 5/99 and the associated confidence interval for the difference was calculated using the method of Miettinen and Nurminen

Comparison groups	Group 3B v Group B_0_1

Number of subjects included in analysis	445
Analysis specification	Pre-specified
Analysis type	other[46]
Method	Miettinen and Nurminen score method
Parameter estimate	vaccine group difference
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	6.2

Notes:

[46] - Vaccine comparison at Day 8 Group 3B vs Day 38 Group B_0_1 (7 days after booster or 2nd dose)

Statistical analysis title	Statistical analysis 6

Statistical analysis description:

1 month post vaccination-The group difference in percentages of subjects with response against N. meningitidis serogroup B indicator strain 5/99 and the associated confidence interval for the difference was calculated using the method of Miettinen and Nurminen

Comparison groups	Group 3B v Group B_0_1
Number of subjects included in analysis	445
Analysis specification	Pre-specified
Analysis type	other[47]
Method	Miettinen and Nurminen score method
Parameter estimate	vaccine group difference
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	4.1

Notes:

[47] - Vaccine comparison at Day 31 Group 3B vs Day 61 Group B_0_1 (1 month after booster or 2nd dose)

Statistical analysis title	Statistical analysis 7

Statistical analysis description:

3 days post vaccination-The group difference in percentages of subjects with response against N. meningitidis serogroup B indicator strain NZ98/254 and the associated confidence interval for the difference was calculated using the method of Miettinen and Nurminen

Comparison groups	Group 3B v Group B_0_1
Number of subjects included in analysis	445
Analysis specification	Pre-specified
Analysis type	other[48]
Method	Miettinen and Nurminen score method
Parameter estimate	vaccine group difference
Point estimate	-26
Confidence interval	
level	95 %
sides	2-sided
lower limit	-36.9
upper limit	-15.7

Notes:

[48] - Vaccine comparison at Day 4 Group 3B vs Day 34 Group B_0_1 (3 days after booster or 2nd dose)

Statistical analysis title	Statistical analysis 8

Statistical analysis description:

7 days post vaccination-The group difference in percentages of subjects with response N. meningitidis serogroup B indicator strain NZ98/254 and the associated confidence interval for the difference was calculated using the method of Miettinen and Nurminen

Comparison groups	Group 3B v Group B_0_1
Number of subjects included in analysis	445
Analysis specification	Pre-specified
Analysis type	other[49]
Method	Miettinen and Nurminen score method
Parameter estimate	vaccine group difference
Point estimate	-5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.1
upper limit	5.8

Notes:

[49] - Vaccine comparison at Day 8 Group 3B vs Day 38 Group B_0_1 (7 days after booster or 2nd dose)

Statistical analysis title	Statistical analysis 9

Statistical analysis description:

1 month post vaccination-The group difference in percentages of subjects with response N. meningitidis serogroup B indicator strain NZ98/254 and the associated confidence interval for the difference was calculated using the method of Miettinen and Nurminen

Comparison groups	Group 3B v Group B_0_1
Number of subjects included in analysis	445
Analysis specification	Pre-specified
Analysis type	other[50]
Method	Miettinen and Nurminen score method
Parameter estimate	vaccine group difference
Point estimate	16
Confidence interval	
level	95 %
sides	2-sided
lower limit	9.8
upper limit	23.3

Notes:

[50] - Vaccine comparison at Day 31 Group 3B vs Day 61 Group B_0_1 (1 month after booster or 2nd dose)

Statistical analysis title	Statistical analysis 10

Statistical analysis description:

3 days post vaccination-The group difference in percentages of subjects with response N. meningitidis serogroup B indicator strain M10713 and the associated confidence interval for the difference was calculated using the method of Miettinen and Nurminen

Comparison groups	Group 3B v Group B_0_1

Number of subjects included in analysis	445
Analysis specification	Pre-specified
Analysis type	other[51]
Method	Miettinen and Nurminen score method
Parameter estimate	vaccine group difference
Point estimate	-4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.4
upper limit	5.8

Notes:

[51] - Vaccine comparison at Day 4 Group 3B vs Day 34 Group B_0_1 (3 days after booster or 2nd dose)

Statistical analysis title	Statistical analysis 11

Statistical analysis description:

7 days post vaccination-The group difference in percentages of subjects with response N. meningitidis serogroup B indicator strain M10713 and the associated confidence interval for the difference was calculated using the method of Miettinen and Nurminen

Comparison groups	Group 3B v Group B_0_1
Number of subjects included in analysis	445
Analysis specification	Pre-specified
Analysis type	other[52]
Method	Miettinen and Nurminen score method
Parameter estimate	vaccine group difference
Point estimate	2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.2
upper limit	7.7

Notes:

[52] - Vaccine comparison at Day 8 Group 3B vs Day 38 Group B_0_1 (7 days after booster or 2nd dose)

Statistical analysis title	Statistical analysis 12

Statistical analysis description:

1 month post vaccination-The group difference in percentages of subjects with response N. meningitidis serogroup B indicator strain M10713 and the associated confidence interval for the difference was calculated using the method of Miettinen and Nurminen

Comparison groups	Group 3B v Group B_0_1
Number of subjects included in analysis	445
Analysis specification	Pre-specified
Analysis type	other[53]
Method	Miettinen and Nurminen score method
Parameter estimate	vaccine group difference
Point estimate	6
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.8
upper limit	10.5

Notes:

[53] - Vaccine comparison at Day 31 Group 3B vs Day 61 Group B_0_1 (1 month after booster or 2nd dose)

Secondary: Percentage of subjects with hSBA ≥1:8 after booster dose/second vaccination of rMenB+OMV NZ

End point title	Percentage of subjects with hSBA ≥1:8 after booster dose/second vaccination of rMenB+OMV NZ

End point description:

Bactericidal activity was measured against each of the four N. meningitidis group B indicator strains H44/76,5/99,NZ98/254 and M10713. On day 1, subjects in the Group B_0_1 were to be randomized into 2 different blood draw schedules according to a 1:1 ratio : 2 blood samples at different time points: Group B_0_1_1: blood draws at 3 and 30 days after the second dose. Group B_0_1_2: blood draws at 7 and 30 days after the second dose.

End point type	Secondary

End point timeframe:

Group 3B: 3, 7 and 30 days after third dose booster; Group B_0_1: At 3 (group B_0_1_1 only), 7 (sub-group B_0_1_2 only) and 30 days post-second dose.

End point values	Group 3B	Group B_0_1		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	242	203		
Units: Percentage of subjects				
number (confidence interval 95%)				
H44/76 3 days post vaccination	30 (24.5 to 36.4)	75 (65.9 to 83.1)		
H44/76 7 days post vaccination	96 (93.1 to 98.3)	97 (91.3 to 99.4)		
H44/76 1 month post vaccination	99 (96.4 to 99.74)	98 (95.0 to 99.5)		
5/99- 3 days post-vaccination	76 (69.4 to 82.2)	83 (72.9 to 89.9)		
5/99- 7 days post-vaccination	100 (98.0 to 100.0)	99 (93.8 to 99.97)		
5/99- 1 month post-vaccination	100 (98.0 to 100.0)	99 (95.9 to 99.86)		
NZ98/254- 3 days post-vaccination	16 (11.4 to 21.2)	42 (32.3 to 51.9)		
NZ98/254- 7 days post-vaccination	67 (60.1 to 72.6)	69 (59.3 to 78.3)		
NZ98/254- 1 month post-vaccination	88 (82.6 to 91.5)	67 (60.1 to 73.4)		
M10713- 3 days post-vaccination	70 (63.5 to 75.4)	73 (63.8 to 81.5)		
M10713- 7 days post-vaccination	95 (92.0 to 97.7)	94 (87.1 to 97.7)		
M10713- 1 month post-vaccination	98 (95.8 to 99.55)	90 (85.2 to 93.9)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

3 days post vaccination-The group difference in percentages of subjects with response against N. meningitidis serogroup B indicator strain H44/76 and the associated confidence interval for the difference was calculated using the method of Miettinen and Nurminen.

Comparison groups	Group B_0_1 v Group 3B
Number of subjects included in analysis	445
Analysis specification	Pre-specified
Analysis type	other[54]
Method	Miettinen and Nurminen score method
Parameter estimate	vaccine group difference
Point estimate	-45
Confidence interval	
level	95 %
sides	2-sided
lower limit	-54.4
upper limit	-34.3

Notes:

[54] - Vaccine comparison at Day 4 Group 3B vs Day 34 Group B_0_1 (3 days after booster or 2nd dose)

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

7 days post vaccination-The group difference in percentages of subjects with response against N. meningitidis serogroup B indicator strain H44/76 and the associated confidence interval for the difference was calculated using the method of Miettinen and Nurminen

Comparison groups	Group B_0_1 v Group 3B
Number of subjects included in analysis	445
Analysis specification	Pre-specified
Analysis type	other[55]
Method	Miettinen and Nurminen score method
Parameter estimate	vaccine group difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.5
upper limit	5.2

Notes:

[55] - Vaccine comparison at Day 8 Group 3B vs Day 38 Group B_0_1 (7 days after booster or 2nd dose)

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

1 month post vaccination-The group difference in percentages of subjects with response against N. meningitidis serogroup B indicator strain H44/76 and the associated confidence interval for the difference was calculated using the method of Miettinen and Nurminen

Comparison groups	Group B_0_1 v Group 3B

Number of subjects included in analysis	445
Analysis specification	Pre-specified
Analysis type	other[56]
Method	Miettinen and Nurminen score method
Parameter estimate	vaccine group difference
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.9
upper limit	3.9

Notes:

[56] - Vaccine comparison at Day 31 Group 3B vs Day 61 Group B_0_1 (1 month after booster or 2nd dose)

Statistical analysis title	Statistical analysis 4

Statistical analysis description:

3 days post vaccination-The group difference in percentages of subjects with response against N. meningitidis serogroup B indicator strain 5/99 and the associated confidence interval for the difference was calculated using the method of Miettinen and Nurminen

Comparison groups	Group B_0_1 v Group 3B
Number of subjects included in analysis	445
Analysis specification	Pre-specified
Analysis type	other[57]
Method	Miettinen and Nurminen score method
Parameter estimate	vaccine group difference
Point estimate	-6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.9
upper limit	4.6

Notes:

[57] - Vaccine comparison at Day 4 Group 3B vs Day 34 Group B_0_1 (3 days after booster or 2nd dose)

Statistical analysis title	Statistical analysis 5

Statistical analysis description:

7 days post vaccination-The group difference in percentages of subjects with response against N. meningitidis serogroup B indicator strain 5/99 and the associated confidence interval for the difference was calculated using the method of Miettinen and Nurminen

Comparison groups	Group B_0_1 v Group 3B
Number of subjects included in analysis	445
Analysis specification	Pre-specified
Analysis type	other[58]
Method	Miettinen and Nurminen score method
Parameter estimate	vaccine group difference
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	6.2

Notes:

[58] - Vaccine comparison at Day 8 Group 3B vs Day 38 Group B_0_1 (7 days after booster or 2nd dose)

Statistical analysis title	Statistical analysis 6

Statistical analysis description:

1 month post vaccination-The group difference in percentages of subjects with response against N. meningitidis serogroup B indicator strain 5/99 and the associated confidence interval for the difference was calculated using the method of Miettinen and Nurminen

Comparison groups	Group B_0_1 v Group 3B
Number of subjects included in analysis	445
Analysis specification	Pre-specified
Analysis type	other[59]
Method	Miettinen and Nurminen score method
Parameter estimate	vaccine group difference
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	4.1

Notes:

[59] - Vaccine comparison at Day 31 Group 3B vs Day 61 Group B_0_1 (1 month after booster or 2nd dose)

Statistical analysis title	Statistical analysis 7

Statistical analysis description:

3 days post vaccination-The group difference in percentages of subjects with response against N. meningitidis serogroup B indicator strain NZ98/254 and the associated confidence interval for the difference was calculated using the method of Miettinen and Nurminen

Comparison groups	Group B_0_1 v Group 3B
Number of subjects included in analysis	445
Analysis specification	Pre-specified
Analysis type	other[60]
Method	Miettinen and Nurminen score method
Parameter estimate	vaccine group difference
Point estimate	-26
Confidence interval	
level	95 %
sides	2-sided
lower limit	-36.6
upper limit	-15.7

Notes:

[60] - Vaccine comparison at Day 4 Group 3B vs Day 34 Group B_0_1 (3 days after booster or 2nd dose)

Statistical analysis title	Statistical analysis 8

Statistical analysis description:

7 days post vaccination-The group difference in percentages of subjects with response against N. meningitidis serogroup B indicator strain NZ98/254 and the associated confidence interval for the difference was calculated using the method of Miettinen and Nurminen

Comparison groups	Group B_0_1 v Group 3B

Number of subjects included in analysis	445
Analysis specification	Pre-specified
Analysis type	other[61]
Method	Miettinen and Nurminen score method
Parameter estimate	vaccine group difference
Point estimate	-3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.3
upper limit	8.5

Notes:

[61] - Vaccine comparison at Day 8 Group 3B vs Day 38 Group B_0_1 (7 days after booster or 2nd dose)

Statistical analysis title	Statistical analysis 9

Statistical analysis description:

1 month post vaccination-The group difference in percentages of subjects with response against N. meningitidis serogroup B indicator strain NZ98/254 and the associated confidence interval for the difference was calculated using the method of Miettinen and Nurminen

Comparison groups	Group B_0_1 v Group 3B
Number of subjects included in analysis	445
Analysis specification	Pre-specified
Analysis type	other[62]
Method	Miettinen and Nurminen score method
Parameter estimate	vaccine group difference
Point estimate	21
Confidence interval	
level	95 %
sides	2-sided
lower limit	12.8
upper limit	28.3

Notes:

[62] - Vaccine comparison at Day 31 Group 3B vs Day 61 Group B_0_1 (1 month after booster or 2nd dose)

Statistical analysis title	Statistical analysis 10

Statistical analysis description:

3 days post vaccination-The group difference in percentages of subjects with response against N. meningitidis serogroup B indicator strain M10713 and the associated confidence interval for the difference was calculated using the method of Miettinen and Nurminen

Comparison groups	Group B_0_1 v Group 3B
Number of subjects included in analysis	445
Analysis specification	Pre-specified
Analysis type	other[63]
Method	Miettinen and Nurminen score method
Parameter estimate	vaccine group difference
Point estimate	-4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.4
upper limit	7.1

Notes:

[63] - Vaccine comparison at Day 4 Group 3B vs Day 34 Group B_0_1 (3 days after booster or 2nd dose)

Statistical analysis title	Statistical analysis 11

Statistical analysis description:

7 days post vaccination-The group difference in percentages of subjects with response against N. meningitidis serogroup B indicator strain M10713 and the associated confidence interval for the difference was calculated using the method of Miettinen and Nurminen

Comparison groups	Group B_0_1 v Group 3B
Number of subjects included in analysis	445
Analysis specification	Pre-specified
Analysis type	other[64]
Method	Miettinen and Nurminen score method
Parameter estimate	vaccine group difference
Point estimate	2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.2
upper limit	8.5

Notes:

[64] - Vaccine comparison at Day 8 Group 3B vs Day 38 Group B_0_1 (7 days after booster or 2nd dose)

Statistical analysis title	Statistical analysis 12

Statistical analysis description:

1 month post vaccination-The group difference in percentages of subjects with response against N. meningitidis serogroup B indicator strain M10713 and the associated confidence interval for the difference was calculated using the method of Miettinen and Nurminen

Comparison groups	Group B_0_1 v Group 3B
Number of subjects included in analysis	445
Analysis specification	Pre-specified
Analysis type	other[65]
Method	Miettinen and Nurminen score method
Parameter estimate	vaccine group difference
Point estimate	8
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.2
upper limit	13.2

Notes:

[65] - Vaccine comparison at Day 31 Group 3B vs Day 61 Group B_0_1 (1 month after booster or 2nd dose)

Secondary: Percentage of subjects with hSBA ≥1:16 after booster dose/second vaccination of rMenB+OMV NZ

End point title	Percentage of subjects with hSBA ≥1:16 after booster dose/second vaccination of rMenB+OMV NZ

End point description:

Bactericidal activity was measured against each of the four N. meningitidis group B indicator strains H44/76,5/99,NZ98/254 and M10713. On day 1, subjects in the Group B_0_1 were to be randomized into 2 different blood draw schedules according to a 1:1 ratio : 2 blood samples at different time points: Group B_0_1_1: blood draws at 3 and 30 days after the second dose. Group B_0_1_2: blood draws at 7

and 30 days after the second dose.

End point type	Secondary

End point timeframe:

Group 3B: 3, 7 and 30 days after third dose booster; Group B_0_1: At 3 (group B_0_1_1 only), 7 (sub-group B_0_1_2 only) and 30 days post-second dose

End point values	Group 3B	Group B_0_1		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	242	203		
Units: Percentage of subjects				
number (confidence interval 95%)				
H44/76 3 days post vaccination	21 (15.7 to 26.3)	50 (40.5 to 60.4)		
H44/76 7 days post vaccination	95 (91.0 to 97.1)	92 (84.5 to 96.4)		
H44/76 1 month post vaccination	99 (96.4 to 99.74)	91 (86.3 to 94.7)		
5/99- 3 days post-vaccination	70 (63.1 to 76.8)	76 (65.1 to 84.2)		
5/99- 7 days post-vaccination	100 (98.0 to 100.0)	99 (93.8 to 99.97)		
5/99- 1 month post-vaccination	100 (98.0 to 100.0)	98 (95.0 to 99.64)		
NZ98/254- 3 days post-vaccination	9 (6.0 to 13.9)	30 (21.0 to 39.2)		
NZ98/254- 7 days post-vaccination	51 (44.5 to 57.7)	47 (36.8 to 57.3)		
NZ98/254- 1 month post-vaccination	81 (75.0 to 85.6)	49 (41.7 to 55.9)		
M10713- 3 days post-vaccination	59 (52.0 to 64.8)	64 (53.9 to 73.0)		
M10713- 7 days post-vaccination	88 (83.2 to 91.8)	88 (79.6 to 93.5)		
M10713- 1 month post-vaccination	95 (91.5 to 97.4)	84 (78.5 to 89.0)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

3 days post vaccination-The group difference in percentages of subjects with response against N. meningitidis serogroup B indicator strain H44/76 and the associated confidence interval for the difference was calculated using the method of Miettinen and Nurminen.

Comparison groups	Group B_0_1 v Group 3B
Number of subjects included in analysis	445
Analysis specification	Pre-specified
Analysis type	other[66]
Method	Miettinen and Nurminen score method
Parameter estimate	vaccine group difference
Point estimate	-30

Confidence interval	
level	95 %
sides	2-sided
lower limit	-40.4
upper limit	-19

Notes:

[66] - Vaccine comparison at Day 4 Group 3B vs Day 34 Group B_0_1 (3 days after booster or 2nd dose)

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

7 days post vaccination-The group difference in percentages of subjects with response against N. meningitidis serogroup B indicator strain H44/76 and the associated confidence interval for the difference was calculated using the method of Miettinen and Nurminen

Comparison groups	Group B_0_1 v Group 3B
Number of subjects included in analysis	445
Analysis specification	Pre-specified
Analysis type	other[67]
Method	Miettinen and Nurminen score method
Parameter estimate	vaccine group difference
Point estimate	3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.6
upper limit	10.3

Notes:

[67] - Vaccine comparison at Day 8 Group 3B vs Day 38 Group B_0_1 (7 days after booster or 2nd dose)

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

1 month post vaccination-The group difference in percentages of subjects with response against N. meningitidis serogroup B indicator strain H44/76 and the associated confidence interval for the difference was calculated using the method of Miettinen and Nurminen

Comparison groups	Group B_0_1 v Group 3B
Number of subjects included in analysis	445
Analysis specification	Pre-specified
Analysis type	other[68]
Method	Miettinen and Nurminen score method
Parameter estimate	vaccine group difference
Point estimate	8
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.9
upper limit	12.5

Notes:

[68] - Vaccine comparison at Day 31 Group 3B vs Day 61 Group B_0_1 (1 month after booster or 2nd dose)

Statistical analysis title	Statistical analysis 4

Statistical analysis description:

3 days post vaccination-The group difference in percentages of subjects with response against N.

meningitidis serogroup B indicator strain 5/99 and the associated confidence interval for the difference was calculated using the method of Miettinen and Nurminen

Comparison groups	Group B_0_1 v Group 3B
Number of subjects included in analysis	445
Analysis specification	Pre-specified
Analysis type	other[69]
Method	Miettinen and Nurminen score method
Parameter estimate	vaccine group difference
Point estimate	-5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16
upper limit	6.5

Notes:

[69] - Vaccine comparison at Day 4 Group 3B vs Day 34 Group B_0_1 (3 days after booster or 2nd dose)

Statistical analysis title	Statistical analysis 5

Statistical analysis description:

7 days post vaccination-The group difference in percentages of subjects with response against N. meningitidis serogroup B indicator strain 5/99 and the associated confidence interval for the difference was calculated using the method of Miettinen and Nurminen

Comparison groups	Group B_0_1 v Group 3B
Number of subjects included in analysis	445
Analysis specification	Pre-specified
Analysis type	other[70]
Method	Miettinen and Nurminen score method
Parameter estimate	vaccine group difference
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	6.2

Notes:

[70] - Vaccine comparison at Day 8 Group 3B vs Day 38 Group B_0_1 (7 days after booster or 2nd dose)

Statistical analysis title	Statistical analysis 6

Statistical analysis description:

1 month post vaccination-The group difference in percentages of subjects with response against N. meningitidis serogroup B indicator strain 5/99 and the associated confidence interval for the difference was calculated using the method of Miettinen and Nurminen

Comparison groups	Group B_0_1 v Group 3B
Number of subjects included in analysis	445
Analysis specification	Pre-specified
Analysis type	other[71]
Method	Miettinen and Nurminen score method
Parameter estimate	vaccine group difference
Point estimate	2

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.33
upper limit	5

Notes:

[71] - Vaccine comparison at Day 31 Group 3B vs Day 61 Group B_0_1 (1 month after booster or 2nd dose)

Statistical analysis title	Statistical analysis 7

Statistical analysis description:

3 days post vaccination-The group difference in percentages of subjects with response against N. meningitidis serogroup B indicator strain NZ98/254 and the associated confidence interval for the difference was calculated using the method of Miettinen and Nurminen.

Comparison groups	Group B_0_1 v Group 3B
Number of subjects included in analysis	445
Analysis specification	Pre-specified
Analysis type	other[72]
Method	Miettinen and Nurminen score method
Parameter estimate	vaccine group difference
Point estimate	-20
Confidence interval	
level	95 %
sides	2-sided
lower limit	-30
upper limit	-11.1

Notes:

[72] - Vaccine comparison at Day 4 Group 3B vs Day 34 Group B_0_1 (3 days after booster or 2nd dose)

Statistical analysis title	Statistical analysis 8

Statistical analysis description:

7 days post vaccination-The group difference in percentages of subjects with response against N. meningitidis serogroup B indicator strain NZ98/254 and the associated confidence interval for the difference was calculated using the method of Miettinen and Nurminen

Comparison groups	Group B_0_1 v Group 3B
Number of subjects included in analysis	445
Analysis specification	Pre-specified
Analysis type	other[73]
Method	Miettinen and Nurminen score method
Parameter estimate	vaccine group difference
Point estimate	4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.6
upper limit	15.7

Notes:

[73] - Vaccine comparison at Day 8 Group 3B vs Day 38 Group B_0_1 (7 days after booster or 2nd dose)

Statistical analysis title	Statistical analysis 9

Statistical analysis description:

1 month post vaccination-The group difference in percentages of subjects with response against N.

meningitidis serogroup B indicator strain NZ98/254 and the associated confidence interval for the difference was calculated using the method of Miettinen and Nurminen

Comparison groups	Group B_0_1 v Group 3B
Number of subjects included in analysis	445
Analysis specification	Pre-specified
Analysis type	other[74]
Method	Miettinen and Nurminen score method
Parameter estimate	vaccine group difference
Point estimate	32
Confidence interval	
level	95 %
sides	2-sided
lower limit	23.2
upper limit	40.2

Notes:

[74] - Vaccine comparison at Day 31 Group 3B vs Day 61 Group B_0_1 (1 month after booster or 2nd dose)

Statistical analysis title	Statistical analysis 10

Statistical analysis description:

3 days post vaccination-The group difference in percentages of subjects with response against N. meningitidis serogroup B indicator strain M10713 and the associated confidence interval for the difference was calculated using the method of Miettinen and Nurminen

Comparison groups	Group B_0_1 v Group 3B
Number of subjects included in analysis	445
Analysis specification	Pre-specified
Analysis type	other[75]
Method	Miettinen and Nurminen score method
Parameter estimate	vaccine group difference
Point estimate	-5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16
upper limit	6

Notes:

[75] - Vaccine comparison at Day 4 Group 3B vs Day 34 Group B_0_1 (3 days after booster or 2nd dose)

Statistical analysis title	Statistical analysis 11

Statistical analysis description:

7 days post vaccination-The group difference in percentages of subjects with response against N. meningitidis serogroup B indicator strain M10713 and the associated confidence interval for the difference was calculated using the method of Miettinen and Nurminen

Comparison groups	Group B_0_1 v Group 3B
Number of subjects included in analysis	445
Analysis specification	Pre-specified
Analysis type	other[76]
Method	Miettinen and Nurminen score method
Parameter estimate	vaccine group difference
Point estimate	0

Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.8
upper limit	8.9

Notes:

[76] - Vaccine comparison at Day 8 Group 3B vs Day 38 Group B_0_1 (7 days after booster or 2nd dose)

Statistical analysis title	Statistical analysis 12

Statistical analysis description:

1 month post vaccination-The group difference in percentages of subjects with response against N. meningitidis serogroup B indicator strain M10713 and the associated confidence interval for the difference was calculated using the method of Miettinen and Nurminen

Comparison groups	Group B_0_1 v Group 3B
Number of subjects included in analysis	445
Analysis specification	Pre-specified
Analysis type	other[77]
Method	Miettinen and Nurminen score method
Parameter estimate	vaccine group difference
Point estimate	11
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.3
upper limit	16.9

Notes:

[77] - Vaccine comparison at Day 31 Group 3B vs Day 61 Group B_0_1 (1 month after booster or 2nd dose)

Secondary: hSBA Geometric Mean Titers prior to booster/second dose of vaccination & post booster/second dose of vaccination.

End point title	hSBA Geometric Mean Titers prior to booster/second dose of vaccination & post booster/second dose of vaccination.

End point description:

Bactericidal activity was measured against each of the four N. meningitidis group B indicator strains H44/76,5/99,NZ98/254 and M10713. On day 1, subjects in the Group B_0_1 were to be randomized into 2 different blood draw schedules according to a 1:1 ratio : 2 blood samples at different time points: Group B_0_1_1: blood draws at 3 and 30 days after the second dose. Group B_0_1_2: blood draws at 7 and 30 days after the second dose.

End point type	Secondary

End point timeframe:

Group 3B: Day 1 (pre-booster dose) and 3, 7 and 30 days after third dose booster; Group B_0_1: Pre 2nd dose and at 3 (group B_0_1_1 only), 7 (group B_0_1_2 only) and 30 days post second dose.

End point values	Group 3B	Group B_0_1		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	242	203		
Units: Titers				
geometric mean (confidence interval 95%)				

H44/76 - pre-vaccination	2.99 (2.41 to 3.70)	17 (14 to 22)		
H44/76 - 3 days post-vacc	3.20 (2.60 to 3.94)	17 (13 to 23)		
H44/76 - 7 days post-vacc	115 (98 to 136)	57 (44 to 73)		
H44/76 - 1 month post-vacc.	196 (170 to 228)	56 (48 to 66)		
5/99- pre-vaccination	24 (18 to 32)	31 (23 to 41)		
5/99- 3 days post-vacc	24 (18 to 31)	27 (19 to 41)		
5/99- 7 days post-vacc	1787 (1477 to 2162)	337 (257 to 442)		
5/99- 1 month post-vacc.	2026 (1714 to 2395)	248 (208 to 295)		
NZ98/254- pre-vaccination	1.57 (1.29 to 1.92)	5.11 (4.10 to 6.38)		
NZ98/254- 3 days post-vacc	1.62 (1.35 to 1.96)	4.45 (3.38 to 5.84)		
NZ98/254- 7 days post-vacc	12 (10 to 15)	12 (8.46 to 16)		
NZ98/254- 1 month post-vacc.	35 (29 to 42)	14 (11 to 17)		
M10713- pre-vaccination	15 (12 to 19)	32 (25 to 41)		
M10713- 3 days post-vacc	16 (13 to 21)	23 (17 to 33)		
M10713- 7 days post-vacc	54 (46 to 62)	45 (36 to 57)		
M10713- 1 month post-vacc.	78 (67 to 92)	41 (35 to 49)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Adjusted geometric mean titers for H44/76 indicator strain were obtained by exponentiating (base 10) the least square means and the lower and upper limits of the 95% confidence intervals of the log-transformed titers obtained from an ANOVA estimation adjusting for vaccine group and country.

Comparison groups	Group B_0_1 v Group 3B
Number of subjects included in analysis	445
Analysis specification	Pre-specified
Analysis type	other[78]
Method	ANOVA
Parameter estimate	vaccine group difference
Point estimate	3.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.85
upper limit	4.29

Notes:

[78] - Vaccine Comparison Day 31 Group 3B vs Day 61 Group B_0_1(1 month after booster or 2nd dose)

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

Adjusted geometric mean titers for 5/99 indicator strain were obtained by exponentiating (base 10) the least square means and the lower and upper limits of the 95% confidence intervals of the log-transformed titers obtained from an ANOVA estimation adjusting for vaccine group and country

Comparison groups	Group B_0_1 v Group 3B

Number of subjects included in analysis	445
Analysis specification	Pre-specified
Analysis type	other[79]
Method	ANOVA
Parameter estimate	vaccine group difference
Point estimate	8.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.51
upper limit	10

Notes:

[79] - Vaccine Comparison Day 31 Group 3B vs Day 61 Group B_0_1(1 month after booster or 2nd dose)

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

Adjusted geometric mean titers for NZ98/254 indicator strain were obtained by exponentiating (base 10) the least square means and the lower and upper limits of the 95% confidence intervals of the log-transformed titers obtained from an ANOVA estimation adjusting for vaccine group and country

Comparison groups	Group B_0_1 v Group 3B
Number of subjects included in analysis	445
Analysis specification	Pre-specified
Analysis type	other[80]
Method	ANOVA
Parameter estimate	vaccine group difference
Point estimate	2.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.98
upper limit	3.36

Notes:

[80] - Vaccine Comparison Day 31 Group 3B vs Day 61 Group B_0_1(1 month after booster or 2nd dose)

Statistical analysis title	Statistical analysis 4

Statistical analysis description:

Adjusted geometric mean titers for M10713 indicator strain were obtained by exponentiating (base 10) the least square means and the lower and upper limits of the 95% confidence intervals of the log-transformed titers obtained from an ANOVA estimation adjusting for vaccine group and country

Comparison groups	Group B_0_1 v Group 3B
Number of subjects included in analysis	445
Analysis specification	Pre-specified
Analysis type	other[81]
Method	ANOVA
Parameter estimate	vaccine group difference
Point estimate	1.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.52
upper limit	2.36

Notes:

[81] - Vaccine Comparison Day 31 Group 3B vs Day 61 Group B_0_1(1 month after booster or 2nd dose)

Secondary: Geometric Mean Ratios (GMRs) of GMTs after booster/second vaccination versus before booster/second vaccination.

End point title	Geometric Mean Ratios (GMRs) of GMTs after booster/second vaccination versus before booster/second vaccination.

End point description:

Bactericidal activity was measured against each of the four N. meningitidis group B indicator strains H44/76,5/99,NZ98/254 and M10713 by calculating the GMRs of GMTs post-vaccination with a booster dose (Group 3B) versus pre-booster dose or second dose (Group B_0_1) of vaccination versus pre-second dose.

End point type	Secondary

End point timeframe:

Group 3B: Day 1 and 30 days after third dose booster; Group B_0_1: 30 days post-first dose and at 30 days post-second dose

End point values	Group 3B	Group B_0_1		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	242	203		
Units: Ratio				
geometric mean (confidence interval 95%)				
H44/76	66 (55 to 79)	3.27 (2.66 to 4.03)		
5/99	85 (65 to 111)	8.10 (6.12 to 11)		
NZ98/25	22 (19 to 27)	2.63 (2.15 to 3.21)		
M10713	5.07 (4.33 to 5.94)	1.27 (1.07 to 1.52)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentages of Subjects with at Least Four-fold Increase in hSBA Titers Pre-booster/Second dose vaccination- compared to 3, 7 and 30 Days Post-booster/Second Vaccination

End point title	Percentages of Subjects with at Least Four-fold Increase in hSBA Titers Pre-booster/Second dose vaccination- compared to 3, 7 and 30 Days Post- booster/Second Vaccination

End point description:

The percentage of subjects with 4-fold rise at three, seven, thirty days post-vaccination with a booster dose (follow-on subjects) /second dose (naive subjects) of rMenB+OMV NZ with respect to day 1 (follow-on subjects) / pre-second dose of rMenB+OMV NZ (naïve subjects). Percentage of subjects with four-fold rise in hSBA titers relative to baseline were defined as: • for a pre-vaccination titer < 4, a post-vaccination titer of at least 16; • for a pre-vaccination titer ≥ 4 but <LLOQ, a post vaccination titer of at least fourfold the LLOQ; • for a pre-vaccination titer ≥LLOQ, a post vaccination titer of at least fourfold the pre-vaccination titer

End point type	Secondary

End point timeframe:

Group 3B: at 3, 7 and 30 days after third dose booster; Group B_0_1: at 3 (group B_0_1_1 only), 7 (group B_0_1_2 only) and 30 days post second dose

End point values	Group 3B	Group B_0_1		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	242	203		
Units: Percentage of subjects				
number (confidence interval 95%)				
H44/76 3 days post vaccination	2 (0.7 to 4.8)	4 (1.0 to 9.5)		
H44/76 - 7 days post-vacc	88 (82.8 to 91.5)	35 (25.4 to 45.0)		
H44/76 - 1 month post-vacc.	96 (93.1 to 98.3)	38 (31.7 to 45.5)		
5/99- 3 days post-vacc	5 (2.0 to 8.8)	6 (2.0 to 13.5)		
5/99- 7 days post-vacc	97 (92.7 to 98.7)	59 (48.2 to 69.8)		
5/99- 1 month post-vacc.	97 (93.5 to 99.1)	64 (56.8 to 71.7)		
NZ98/254- 3 days post-vacc	2 (0.7 to 5.0)	2 (0.23 to 6.8)		
NZ98/254- 7 days post-vacc	55 (48.3 to 61.5)	19 (11.4 to 27.7)		
NZ98/254- 1 month post-vacc.	81 (75.3 to 85.8)	27 (21.3 to 34.1)		
M10713- 3 days post-vacc	3 (0.9 to 5.4)	0 (0.0 to 3.5)		
M10713- 7 days post-vacc	34 (27.8 to 40.1)	6 (2.3 to 13.0)		
M10713- 1 month post-vacc.	49 (42.3 to 55.3)	9 (5.8 to 14.3)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

3 days post vaccination-The group difference in percentages of subjects with response against N. meningitidis serogroup B indicator strain H44/76 and the associated confidence interval for the difference was calculated using the method of Miettinen and Nurminen

Comparison groups	Group B_0_1 v Group 3B
Number of subjects included in analysis	445
Analysis specification	Pre-specified
Analysis type	other[82]
Method	Miettinen and Nurminen score method
Parameter estimate	Vaccine group difference
Point estimate	-2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.5
upper limit	1.8

Notes:

[82] - 3 Days Post Booster/Second Vaccination. Four-fold Increase (Group 3B vs. Group B_0_1) Difference

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

7 days post vaccination-The group difference in percentages of subjects with response against N. meningitidis serogroup B indicator strain H44/76 and the associated confidence interval for the difference was calculated using the method of Miettinen and Nurminen.

Comparison groups	Group B_0_1 v Group 3B
Number of subjects included in analysis	445
Analysis specification	Pre-specified
Analysis type	other[83]
Method	Miettinen and Nurminen score method
Parameter estimate	vaccine group difference
Point estimate	53
Confidence interval	
level	95 %
sides	2-sided
lower limit	42.1
upper limit	62.5

Notes:

[83] - 7 Days Post Booster/Second Vaccination. Four-fold Increase (Group 3B vs. Group B_0_1) Difference

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

1 month post vaccination-The group difference in percentages of subjects with response against N. meningitidis serogroup B indicator strain H44/76 and the associated confidence interval for the difference was calculated using the method of Miettinen and Nurminen.

Comparison groups	Group B_0_1 v Group 3B
Number of subjects included in analysis	445
Analysis specification	Pre-specified
Analysis type	other[84]
Method	Miettinen and Nurminen score method
Parameter estimate	vaccine group difference
Point estimate	58
Confidence interval	
level	95 %
sides	2-sided
lower limit	50.5
upper limit	64.7

Notes:

[84] - 1 Month Post Booster/Second Vaccination. Four-fold Increase (Group 3B vs. Group B_0_1) Difference

Statistical analysis title	Statistical analysis 4

Statistical analysis description:

3 days post vaccination-The group difference in percentages of subjects with response against N. meningitidis serogroup B indicator strain 5/99 and the associated confidence interval for the difference was calculated using the method of Miettinen and Nurminen.

Comparison groups	Group B_0_1 v Group 3B

Number of subjects included in analysis	445
Analysis specification	Pre-specified
Analysis type	other[85]
Method	Miettinen and Nurminen score method
Parameter estimate	vaccine group difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.1
upper limit	4

Notes:

[85] - 3 Days Post Booster/Second Vaccination. Four-fold Increase (Group 3B vs. Group B_0_1) Difference

Statistical analysis title	Statistical analysis 5

Statistical analysis description:

7 days post vaccination-The group difference in percentages of subjects with response against N. meningitidis serogroup B indicator strain 5/99 and the associated confidence interval for the difference was calculated using the method of Miettinen and Nurminen

Comparison groups	Group B_0_1 v Group 3B
Number of subjects included in analysis	445
Analysis specification	Pre-specified
Analysis type	other[86]
Method	Miettinen and Nurminen score method
Parameter estimate	vaccine group difference
Point estimate	37
Confidence interval	
level	95 %
sides	2-sided
lower limit	27
upper limit	48.1

Notes:

[86] - 7 Days Post Booster/Second Vaccination. Four-fold Increase (Group 3B vs. Group B_0_1) Difference

Statistical analysis title	Statistical analysis 6

Statistical analysis description:

1 month post vaccination-The group difference in percentages of subjects with response against N. meningitidis serogroup B indicator strain 5/99 and the associated confidence interval for the difference was calculated using the method of Miettinen and Nurminen.

Comparison groups	Group B_0_1 v Group 3B
Number of subjects included in analysis	445
Analysis specification	Pre-specified
Analysis type	other[87]
Method	Miettinen and Nurminen score method
Parameter estimate	Vaccine group difference
Point estimate	33
Confidence interval	
level	95 %
sides	2-sided
lower limit	25.2
upper limit	40.4

Notes:

[87] - 1 Month Post Booster/Second Vaccination. Four-fold Increase (Group 3B vs. Group B_0_1) Difference

Statistical analysis title	Statistical analysis 7

Statistical analysis description:

3 days post vaccination-The group difference in percentages of subjects with response against N. meningitidis serogroup B indicator strain NZ98/254 and the associated confidence interval for the difference was calculated using the method of Miettinen and Nurminen

Comparison groups	Group B_0_1 v Group 3B
Number of subjects included in analysis	445
Analysis specification	Pre-specified
Analysis type	other[88]
Method	Miettinen and Nurminen score method
Parameter estimate	vaccine group difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.7
upper limit	3.4

Notes:

[88] - 3 Days Post Booster/Second Vaccination. Four-fold Increase (Group 3B vs. Group B_0_1) Difference

Statistical analysis title	Statistical analysis 8

Statistical analysis description:

7 days post vaccination-The group difference in percentages of subjects with response against N. meningitidis serogroup B indicator strain NZ98/254 and the associated confidence interval for the difference was calculated using the method of Miettinen and Nurminen.

Comparison groups	Group B_0_1 v Group 3B
Number of subjects included in analysis	445
Analysis specification	Pre-specified
Analysis type	other[89]
Method	Miettinen and Nurminen score method
Parameter estimate	Vaccine group difference
Point estimate	36
Confidence interval	
level	95 %
sides	2-sided
lower limit	25.6
upper limit	45.7

Notes:

[89] - 7 Days Post Booster/Second Vaccination. Four-fold Increase (Group 3B vs. Group B_0_1) Difference

Statistical analysis title	Statistical analysis 9

Statistical analysis description:

1 month post vaccination-The group difference in percentages of subjects with response against N. meningitidis serogroup B indicator strain NZ98/254 and the associated confidence interval for the difference was calculated using the method of Miettinen and Nurminen.

Comparison groups	Group B_0_1 v Group 3B

Number of subjects included in analysis	445
Analysis specification	Pre-specified
Analysis type	other[90]
Method	Miettinen and Nurminen score method
Parameter estimate	vaccine group difference
Point estimate	54
Confidence interval	
level	95 %
sides	2-sided
lower limit	45.2
upper limit	61.1

Notes:

[90] - 1 Month Post Booster/Second Vaccination. Four-fold Increase (Group 3B vs. Group B_0_1) Difference

Statistical analysis title	Statistical analysis 10

Statistical analysis description:

3 days post vaccination-The group difference in percentages of subjects with response against N. meningitidis serogroup B indicator strain M10713 and the associated confidence interval for the difference was calculated using the method of Miettinen and Nurminen

Comparison groups	Group B_0_1 v Group 3B
Number of subjects included in analysis	445
Analysis specification	Pre-specified
Analysis type	other[91]
Method	Miettinen and Nurminen score method
Parameter estimate	vaccine group difference
Point estimate	3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	5.4

Notes:

[91] - 3 Days Post Booster/Second Vaccination. Four-fold Increase (Group 3B vs. Group B_0_1) Difference

Statistical analysis title	Statistical analysis 11

Statistical analysis description:

7 days post vaccination-The group difference in percentages of subjects with response against N. meningitidis serogroup B indicator strain M10713 and the associated confidence interval for the difference was calculated using the method of Miettinen and Nurminen.

Comparison groups	Group B_0_1 v Group 3B
Number of subjects included in analysis	445
Analysis specification	Pre-specified
Analysis type	other[92]
Method	Miettinen and Nurminen score method
Parameter estimate	vaccine group difference
Point estimate	28
Confidence interval	
level	95 %
sides	2-sided
lower limit	19.1
upper limit	34.9

Notes:

[92] - 7 Days Post Booster/Second Vaccination. Four-fold Increase (Group 3B vs. Group B_0_1) Difference

Statistical analysis title	Statistical analysis 12

Statistical analysis description:

1 month post vaccination-The group difference in percentages of subjects with response against N. meningitidis serogroup B indicator strain M10713 and the associated confidence interval for the difference was calculated using the method of Miettinen and Nurminen

Comparison groups	Group B_0_1 v Group 3B
Number of subjects included in analysis	445
Analysis specification	Pre-specified
Analysis type	other[93]
Method	Miettinen and Nurminen score method
Parameter estimate	vaccine group difference
Point estimate	39
Confidence interval	
level	95 %
sides	2-sided
lower limit	31.6
upper limit	46.6

Notes:

[93] - 1 Month Post Booster/Second Vaccination. Four-fold Increase (Group 3B vs. Group B_0_1) Difference

Secondary: Percentage of subjects with hSBA ≥1:5 after second vaccination of rMenB+OMV NZ

End point title	Percentage of subjects with hSBA ≥1:5 after second vaccination of rMenB+OMV NZ[94]

End point description:

Bactericidal activity was measured against each of the four N. meningitidis group B indicator strains H44/76,5/99,NZ98/254 and M10713. Only subjects receiving a second vaccination (group B_0_1) were assessed for this outcome measure.

End point type	Secondary

End point timeframe:

At Day 61 (30 days post second dose of vaccination.)

Notes:

[94] - 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: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

End point values	Group B_0_1			
Subject group type	Reporting group			
Number of subjects analysed	215			
Units: Percentage of subjects				
number (confidence interval 95%)				
H44/76	99 (96.7 to 99.89)			
5/99	98 (95.6 to 99.68)			
NZ98/254	77 (70.5 to 82.2)			

M10713	93 (88.7 to 96.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with hSBA ≥1:8 after second vaccination of rMenB+OMV NZ.

End point title	Percentage of subjects with hSBA ≥1:8 after second vaccination of rMenB+OMV NZ.[95]

End point description:

Bactericidal activity was measured against each of the four N. meningitidis group B indicator strains H44/76,5/99,NZ98/254 and M10713. Only subjects receiving a second vaccination (group B_0_1) were assessed for this outcome measure.

End point type	Secondary

End point timeframe:

At Day 61 (30 days post second vaccination)

Notes:

[95] - 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: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

End point values	Group B_0_1			
Subject group type	Reporting group			
Number of subjects analysed	215			
Units: Percentage of subjects				
number (confidence interval 95%)				
H44/76	98 (95.3 to 99.5)			
5/99	98 (95.6 to 99.68)			
NZ98/254	67 (60.3 to 73.2)			
M10713	90 (85.4 to 93.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with hSBA ≥1:16 after second vaccination of rMenB+OMV NZ.

End point title	Percentage of subjects with hSBA ≥1:16 after second vaccination of rMenB+OMV NZ.[96]

End point description:

Bactericidal activity was measured against each of the four N. meningitidis group B indicator strains H44/76,5/99,NZ98/254 and M10713. Only subjects receiving a second vaccination (group B_0_1) were assessed for this outcome measure.

End point type	Secondary

End point timeframe:

At Day 61 (30 days post second vaccination)

Notes:

[96] - 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: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

End point values	Group B_0_1			
Subject group type	Reporting group			
Number of subjects analysed	215			
Units: Percentage of subjects				
number (confidence interval 95%)				
H44/76	91 (86.0 to 94.2)			
5/99	98 (94.8 to 99.4)			
NZ98/254	48 (41.5 to 55.3)			
M10713	84 (78.5 to 88.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: hSBA Geometric Mean Titers (GMTs) after second vaccination of rMenB+OMV NZ.

End point title	hSBA Geometric Mean Titers (GMTs) after second vaccination of rMenB+OMV NZ.[97]

End point description:

Bactericidal activity was measured against each of the four N. meningitidis group B indicator strains H44/76,5/99,NZ98/254 and M10713. Only subjects receiving a second vaccination (group B_0_1) were assessed for this outcome measure.

End point type	Secondary

End point timeframe:

At Day 1 & Day 61 (30 days post second dose of vaccination)

Notes:

[97] - 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: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

End point values	Group B_0_1			
Subject group type	Reporting group			
Number of subjects analysed	215			
Units: Titers				
geometric mean (confidence interval 95%)				
H44/76 Day 1	1.32 (1.18 to 1.47)			
H44/76 1 month post 2nd vaccination	61 (53 to 70)			
5/99 Day 1	1.63 (1.35 to 1.96)			
5/99 1 month post 2nd vaccination	257 (217 to 305)			
NZ98/254 Day 1	1.28 (1.15 to 1.42)			
NZ98/254 1 month post 2nd vaccination	14 (11 to 17)			
M10713 Day 1	14 (11 to 18)			
M10713 1 month post 2nd vaccination	46 (38 to 55)			

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric mean ratio (GMRs) of GMTs one month post second vaccination versus pre vaccination at Day 1

End point title	Geometric mean ratio (GMRs) of GMTs one month post second vaccination versus pre vaccination at Day 1[98]

End point description:

Bactericidal activity was measured against each of the four N. meningitidis group B indicator strains H44/76,5/99,NZ98/254 and M10713. Only subjects receiving a second vaccination (group B_0_1) were assessed for this outcome measure.

End point type	Secondary

End point timeframe:

At Day 1 & Day 61 (30 days post 2nd vaccination)

Notes:

[98] - 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: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

End point values	Group B_0_1			
Subject group type	Reporting group			
Number of subjects analysed	215			
Units: Ratio				
geometric mean (confidence interval 95%)				
H44/76	46 (39 to 54)			
5/99	156 (117 to 209)			
NZ98/254	11 (8.88 to 14)			
M10713	3.23 (2.76 to 3.77)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentages of Subjects with at Least Four-fold Increase in hSBA Titers at pre-First Vaccination compared to One Month Post-Second Vaccination

End point title	Percentages of Subjects with at Least Four-fold Increase in hSBA Titers at pre-First Vaccination compared to One Month Post-Second Vaccination[99]

End point description:

The percentage of subjects with 4-fold rise at one month post-vaccination with a second dose (naïve subjects) of rMenB+OMV NZ with respect to day 1, to each and any one, two, three or all 4 indicator strains. Percentage of subjects with four-fold rise in hSBA titers relative to baseline were defined as: • for a pre-vaccination titer < 4, a post-vaccination titer of at least 16; • for a pre-vaccination titer ≥ 4 but <LLOQ, a post vaccination titer of at least fourfold the LLOQ; • for a pre-vaccination titer ≥LLOQ, a post vaccination titer of at least fourfold the pre-vaccination titer. Only subjects receiving the second dose of vaccination(group B_0_1) were considered for this outcome measure.

End point type	Secondary

End point timeframe:

At Day 61 (30 days post second dose of vaccination)

Notes:

[99] - 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: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

End point values	Group B_0_1			
Subject group type	Reporting group			
Number of subjects analysed	215			
Units: Percentage of Subjects				
number (confidence interval 95%)				
H44/76	95 (91.6 to 97.7)			
5/99	97 (92.9 to 98.8)			
NZ98/254	67 (59.9 to 73)			
M10713	35 (28.2 to 41.4)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Solicited AEs were collected until 7 days after vaccinations. Unsolicited AEs were collected 30 days after vaccination at day 31 (all subjects) and at day 61 (group B_0_1 subjects only).	
Adverse event reporting additional description:	
Serious Adverse Events (SAEs) were collected until study termination (1 month for group 3B subjects/ 2 months for group B_0_1 subjects)	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups	
Reporting group title	Group B_0_1
Reporting group description:	
Subjects who received two doses of rMenB+OMV NZ at a 0 and 1 month schedule and had blood collected at baseline, 30 days after the first dose and 3 or 7, and 30 days after the second dose.	
Reporting group title	Group 3B
Reporting group description:	
Subjects who received a third dose booster of rMenB+OMV NZ at 4 to 7.5 years after the last dose received during studies V72P10 (NCT00661713) or V72_41(NCT0142384), and had blood collected at baseline and at 3, 7 and 30 days after the third dose booster.	

Serious adverse events	Group B_0_1	Group 3B	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 255 (0.39%)	0 / 275 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 255 (0.39%)	0 / 275 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Group B_0_1	Group 3B	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	253 / 255 (99.22%)	266 / 275 (96.73%)	
Nervous system disorders			

Headache			
subjects affected / exposed	126 / 255 (49.41%)	150 / 275 (54.55%)	
occurrences (all)	442	361	
General disorders and administration site conditions			
Injection site pain			
subjects affected / exposed	251 / 255 (98.43%)	259 / 275 (94.18%)	
occurrences (all)	2029	1088	
Injection site erythema			
subjects affected / exposed	135 / 255 (52.94%)	162 / 275 (58.91%)	
occurrences (all)	724	575	
Fatigue			
subjects affected / exposed	141 / 255 (55.29%)	156 / 275 (56.73%)	
occurrences (all)	489	394	
Injection site induration			
subjects affected / exposed	136 / 255 (53.33%)	135 / 275 (49.09%)	
occurrences (all)	834	548	
Injection site swelling			
subjects affected / exposed	111 / 255 (43.53%)	123 / 275 (44.73%)	
occurrences (all)	675	475	
Pyrexia			
subjects affected / exposed	9 / 255 (3.53%)	17 / 275 (6.18%)	
occurrences (all)	16	22	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	53 / 255 (20.78%)	56 / 275 (20.36%)	
occurrences (all)	128	113	
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	100 / 255 (39.22%)	121 / 275 (44.00%)	
occurrences (all)	313	291	
Arthralgia			
subjects affected / exposed	63 / 255 (24.71%)	85 / 275 (30.91%)	
occurrences (all)	212	203	
Infections and infestations			
Viral upper respiratory tract infection			

subjects affected / exposed occurrences (all)	23 / 255 (9.02%) 26	13 / 275 (4.73%) 13	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported