Clinical trial results:
A Phase II, Randomized, Open label, Multi-center Study to Assess the Immunogenicity and Safety of Meningococcal ABCWY Vaccine and of rMenB+OMV NZ and MenACWY Administered Concomitantly in the Same Arm, in Two Separate Arms, or Alone in Healthy Adults 10-25 Years of Age

Summary

EudraCT number	2017-005128-12
Trial protocol	CZ
Global end of trial date	05 July 2019

Results information

Result version number	v2 (current)
This version publication date	26 February 2020
First version publication date	22 December 2019
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	208205

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03587207
WHO universal trial number (UTN)	-
Other trial identifiers	V102_19: Novartis Identifier

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline
Sponsor organisation address	Rue de l'Institut 89, Rixensart, Belgium, B-1330
Public contact	GSK Response Center, GlaxoSmithKline, 044 2089-904466, GSKClinicalSupportHD@gsk.com
Scientific contact	GSK Response Center, GlaxoSmithKline, 044 2089-904466, 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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	06 September 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 December 2018
Global end of trial reached?	Yes
Global end of trial date	05 July 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the immune response to 2 doses of MenABCWY, rMenB+OMV NZ, or rMenB+OMV NZ and MenACWY administered concomitantly in the same arm or in 2 different arms, and to a single dose of MenACWY at 1 month after the last vaccination

Protection of trial subjects:

All subjects were observed for at least 30 minutes after the administration of vaccines with appropriate medical treatment readily available in case of anaphylaxis. Vaccines were administered by qualified and trained personnel. Vaccines were administered only to eligible subjects who had no contraindications to any components of the vaccine. Subjects were followed-up until 30 days after the last vaccination.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 July 2018
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	Czech Republic: 520
Worldwide total number of subjects	520
EEA total number of subjects	520

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)	67
Adolescents (12-17 years)	189
Adults (18-64 years)	264
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were recruited from 1 center at Czechia.

Pre-assignment

Screening details:

Out of the total 520 subjects enrolled in this study, 500 subjects received the vaccination. Among the 20 subjects that were not vaccinated, 15 did not fuflill eligibility criteria and 5 were excluded due to other reasons.

Pre-assignment period milestones

Number of subjects started	520
Number of subjects completed	500

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Other reasons: 5
Reason: Number of subjects	Eligibility criteria not fulfilled: 15

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	MenABCWY Group

Arm description:

Healthy subjects between, and including, 10 to 25 years of age at the time of the first vaccination (equally distributed across the 2 age strata of 10 to 17 years and 18 to 25 years) received one dose of MenABCWY twice, 2 months apart (Day 1 and Day 61).

Arm type	Experimental
Investigational medicinal product name	MenABCWY vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and suspension for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Two doses administered intramuscularly in the deltoid region of the non-dominant arm.

Arm title	rMenBOMV+ACWY_S Group

Arm description:

Healthy subjects between, and including, 10 to 25 years of age at the time of the first vaccination (equally distributed across the 2 age strata of 10 to 17 years and 18 to 25 years) concomitantly received one dose of rMenB+OMV NZ (Bexsero) and one dose of MenACWY (Menveo) in the same arm twice, 2 months apart (Day 1 and Day 61).

Arm type	Active comparator

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

Dosage and administration details:

Two doses administered 2 months apart intramuscularly in the deltoid region of the non-dominant arm to subjects randomized to the rMenBOMV+ACWY_S Group, rMenBOMV+ACWY_D Group and rMenBOMV Group

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

Dosage and administration details:

Two doses administered intramuscularly in the deltoid region of the dominant/non-dominant arm to subjects randomized to the rMenBOMV+ACWY_S Group and rMenBOMV+ACWY_D Group and one dose administered intramuscularly in the deltoid region of the dominant/non-dominant arm to subjects randomized to the MenACWY Group

Arm title	rMenBOMV+ACWY_D Group

Arm description:

Healthy subjects between, and including, 10 to 25 years of age at the time of the first vaccination (equally distributed across the 2 age strata of 10 to 17 years and 18 to 25 years) concomitantly received one dose of rMenB+OMV NZ (Bexsero) and one dose of MenACWY (Menveo) in 2 different arms twice, 2 months apart (Day 1 and Day 61).

Arm type	Active comparator
Investigational medicinal product name	rMenB+OMV NZ (Bexsero) vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Two doses administered 2 months apart intramuscularly in the deltoid region of the non-dominant arm to subjects randomized to the rMenBOMV+ACWY_S Group, rMenBOMV+ACWY_D Group and rMenBOMV Group

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

Dosage and administration details:

Two doses administered intramuscularly in the deltoid region of the dominant/non-dominant arm to subjects randomized to the rMenBOMV+ACWY_S Group and rMenBOMV+ACWY_D Group and one dose administered intramuscularly in the deltoid region of the dominant/non-dominant arm to subjects randomized to the MenACWY Group

Arm title	rMenBOMV Group

Arm description:

Healthy subjects between, and including, 10 to 25 years of age at the time of the first vaccination (equally distributed across the 2 age strata of 10 to 17 years and 18 to 25 years) received one dose of rMenB+OMV NZ (Bexsero) twice, 2 months apart (Day 1 and Day 61).

Arm type	Active comparator

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

Dosage and administration details:

Two doses administered 2 months apart intramuscularly in the deltoid region of the non-dominant arm to subjects randomized to the rMenBOMV+ACWY_S Group, rMenBOMV+ACWY_D Group and rMenBOMV Group

Arm title	MenACWY Group

Arm description:

Healthy subjects between, and including, 10 to 25 years of age at the time of the first vaccination (equally distributed across the 2 age strata of 10 to 17 years and 18 to 25 years) received one dose of MenACWY (Menveo) once at Day 1, which was the first and last vaccination for MenACWY group.

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

Dosage and administration details:

Two doses administered intramuscularly in the deltoid region of the dominant/non-dominant arm to subjects randomized to the rMenBOMV+ACWY_S Group and rMenBOMV+ACWY_D Group and one dose administered intramuscularly in the deltoid region of the dominant/non-dominant arm to subjects randomized to the MenACWY Group

Number of subjects in period 1[1]	MenABCWY Group	rMenBOMV+ACWY_S Group	rMenBOMV+ACWY_D Group
Started	100	104	100
Completed	100	104	100

Number of subjects in period 1[1]	rMenBOMV Group	MenACWY Group
Started	94	102
Completed	94	102

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: The number of subjects reported in the baseline period represent the total exposed set (500), which is different to the worldwide enrolled set (520)

Baseline characteristics

Reporting groups	
Reporting group title	MenABCWY Group
Reporting group description:	
Healthy subjects between, and including, 10 to 25 years of age at the time of the first vaccination (equally distributed across the 2 age strata of 10 to 17 years and 18 to 25 years) received one dose of MenABCWY twice, 2 months apart (Day 1 and Day 61).	
Reporting group title	rMenBOMV+ACWY_S Group
Reporting group description:	
Healthy subjects between, and including, 10 to 25 years of age at the time of the first vaccination (equally distributed across the 2 age strata of 10 to 17 years and 18 to 25 years) concomitantly received one dose of rMenB+OMV NZ (Bexsero) and one dose of MenACWY (Menveo) in the same arm twice, 2 months apart (Day 1 and Day 61).	
Reporting group title	rMenBOMV+ACWY_D Group
Reporting group description:	
Healthy subjects between, and including, 10 to 25 years of age at the time of the first vaccination (equally distributed across the 2 age strata of 10 to 17 years and 18 to 25 years) concomitantly received one dose of rMenB+OMV NZ (Bexsero) and one dose of MenACWY (Menveo) in 2 different arms twice, 2 months apart (Day 1 and Day 61).	
Reporting group title	rMenBOMV Group
Reporting group description:	
Healthy subjects between, and including, 10 to 25 years of age at the time of the first vaccination (equally distributed across the 2 age strata of 10 to 17 years and 18 to 25 years) received one dose of rMenB+OMV NZ (Bexsero) twice, 2 months apart (Day 1 and Day 61).	
Reporting group title	MenACWY Group
Reporting group description:	
Healthy subjects between, and including, 10 to 25 years of age at the time of the first vaccination (equally distributed across the 2 age strata of 10 to 17 years and 18 to 25 years) received one dose of MenACWY (Menveo) once at Day 1, which was the first and last vaccination for MenACWY group.	

Reporting group values	MenABCWY Group	rMenBOMV+ACWY_S Group	rMenBOMV+ACWY_D Group
Number of subjects	100	104	100
Age categorical Units: Subjects			
Children and Adolescents (10-17 years)	53	50	48
Adults (18-25 years)	47	54	52
Age Continuous Units: Years			
arithmetic mean	17.1	16.9	17.1
standard deviation	± 4.34	± 4.28	± 4.49
Sex: Female, Male Units: Subjects			
Female	47	48	49
Male	53	56	51
Race/Ethnicity, Customized Units: Subjects			
WHITE	100	104	100

Reporting group values	rMenBOMV Group	MenACWY Group	Total
Number of subjects	94	102	500

Age categorical Units: Subjects			
Children and Adolescents (10-17 years)	49	50	250
Adults (18-25 years)	45	52	250
Age Continuous Units: Years			
arithmetic mean	17.4	17.1	
standard deviation	± 4.64	± 4.57	-
Sex: Female, Male Units: Subjects			
Female	53	49	246
Male	41	53	254
Race/Ethnicity, Customized Units: Subjects			
WHITE	94	102	500

End points

End points reporting groups

Reporting group title	MenABCWY Group
Reporting group description:	
Healthy subjects between, and including, 10 to 25 years of age at the time of the first vaccination (equally distributed across the 2 age strata of 10 to 17 years and 18 to 25 years) received one dose of MenABCWY twice, 2 months apart (Day 1 and Day 61).	
Reporting group title	rMenBOMV+ACWY_S Group
Reporting group description:	
Healthy subjects between, and including, 10 to 25 years of age at the time of the first vaccination (equally distributed across the 2 age strata of 10 to 17 years and 18 to 25 years) concomitantly received one dose of rMenB+OMV NZ (Bexsero) and one dose of MenACWY (Menveo) in the same arm twice, 2 months apart (Day 1 and Day 61).	
Reporting group title	rMenBOMV+ACWY_D Group
Reporting group description:	
Healthy subjects between, and including, 10 to 25 years of age at the time of the first vaccination (equally distributed across the 2 age strata of 10 to 17 years and 18 to 25 years) concomitantly received one dose of rMenB+OMV NZ (Bexsero) and one dose of MenACWY (Menveo) in 2 different arms twice, 2 months apart (Day 1 and Day 61).	
Reporting group title	rMenBOMV Group
Reporting group description:	
Healthy subjects between, and including, 10 to 25 years of age at the time of the first vaccination (equally distributed across the 2 age strata of 10 to 17 years and 18 to 25 years) received one dose of rMenB+OMV NZ (Bexsero) twice, 2 months apart (Day 1 and Day 61).	
Reporting group title	MenACWY Group
Reporting group description:	
Healthy subjects between, and including, 10 to 25 years of age at the time of the first vaccination (equally distributed across the 2 age strata of 10 to 17 years and 18 to 25 years) received one dose of MenACWY (Menveo) once at Day 1, which was the first and last vaccination for MenACWY group.	

Primary: human Serum Bactericidal Activity (hSBA) Adjusted Geometric Mean Titers (GMTs) against all of N. meningitidis serogroup B test strains (pooled), one month after last vaccination.

End point title	human Serum Bactericidal Activity (hSBA) Adjusted Geometric Mean Titers (GMTs) against all of N. meningitidis serogroup B test strains (pooled), one month after last vaccination.[1]
End point description:	
hSBA titers against all of N. meningitidis serogroup B test strains were calculated in terms of GMTs. Serogroup B strains tested were M14459 (factor H binding protein; fHbp), 96217 (Neisserial adhesin A; NadA), NZ98/254 (PorA), and M070241084 (Neisseria heparin binding antigen; NHBA). The serogroup B strains were grouped together to perform a pooled analysis. Adjusted means were obtained from ANCOVA model fitted to all of the Serogroup B test strains, study group, test strain and center as fixed effects; zero-centered pre-vaccination log-transformed titer was included as a continuous covariate. Analysis was performed on PPS for immunogenicity that included subjects who had no major protocol violations and whose assay results were available for at least 1 serogroup or B strain at Day 91 for all study groups except for MenACWY group that was not considered for this analysis as only serogroup B strains were assessed in this outcome measure.	
End point type	Primary
End point timeframe:	
1 month after last vaccination i.e.: at Day 91 for all groups except for the MenACWY Group	

Notes:

[1] - 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: MenACWY group was not considered for this analysis as only serogroup B strains were assessed in this outcome measure.

End point values	MenABCWY Group	rMenBOMV+ACWY_S Group	rMenBOMV+ACWY_D Group	rMenBOMV Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	98	100	97	90
Units: titers				
geometric mean (confidence interval 80%)	31.84 (28.18 to 35.98)	38.48 (34.23 to 43.26)	40.08 (35.44 to 45.33)	42.38 (37.31 to 48.13)

Statistical analyses

Statistical analysis title	Immune interference-Pooled B strains

Statistical analysis description:

Immune interference due to stress to lymph nodes (lymph-node effect) in rMenBOMV+ACWY_S versus rMenBOMV+ACWY_D study groups, on the pooled B strains, one month after last vaccination.

Comparison groups	rMenBOMV+ACWY_S Group v rMenBOMV+ACWY_D Group
Number of subjects included in analysis	197
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Geometric mean ratio
Point estimate	0.96
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.83
upper limit	1.1

Primary: hSBA Adjusted GMTs against each of the N. meningitidis serogroup B test strains and N. meningitidis serogroups A, C, W-135, and Y, one month after last vaccination

End point title	hSBA Adjusted GMTs against each of the N. meningitidis serogroup B test strains and N. meningitidis serogroups A, C, W-135, and Y, one month after last vaccination

End point description:

hSBA titers against each of the N. meningitidis serogroup B test strains and N. meningitidis serogroups A, C, W-135, and Y were calculated in terms of GMTs. Serogroup B strains tested were M14459 (factor H binding protein; fHbp), 96217 (Neisserial adhesin A; NadA), NZ98/254 (PorA), and M070241084 (Neisseria heparin binding antigen; NHBA). Adjusted means were obtained from ANCOVA model fitted to each Serogroup (Strain) individually, study group and center as fixed effects and zero-centered pre-vaccination log-transformed titer as a continuous covariate. Analysis was performed on PPS for immunogenicity that included subjects who had no major protocol violations and whose assay results were available for at least 1 serogroup or B strain at Day 91 for all study groups except MenACWY Group or at Day 31 for the MenACWY Group.

End point type	Primary

End point timeframe:

1 month after last vaccination i.e.: at Day 91 for all groups except the MenACWY Group, and at Day 31 for the MenACWY Group.

End point values	MenABCWY Group	rMenBOMV+ACWY_S Group	rMenBOMV+ACWY_D Group	rMenBOMV Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	98	101	97	90
Units: titers				
geometric mean (confidence interval 80%)				
M14459 (N-97,100,96,90,97)	23.91 (20.52 to 27.86)	23.34 (20.16 to 27.01)	23.23 (19.91 to 27.10)	22.87 (19.52 to 26.80)
96217 (N-98,100,97,90,96)	81.09 (69.24 to 94.97)	102.68 (88.24 to 119.50)	97.54 (83.18 to 114.39)	113.54 (96.25 to 133.93)
NZ98/254 (N-98,100,97,89,97)	12.97 (10.89 to 15.45)	16.39 (13.86 to 19.39)	21.12 (17.71 to 25.18)	20.97 (17.47 to 25.16)
M07-0241084(N-98,100,96,89,95)	13.08 (11.09 to 15.43)	18.00 (15.35 to 21.11)	22.59 (19.12 to 26.69)	25.34 (21.30 to 30.13)
Meningitis A(N-97,101,97,90,93)	104.90 (87.02 to 126.47)	187.52 (156.94 to 224.05)	204.01 (169.06 to 246.18)	94.91 (78.26 to 115.12)
Meningitis C (N-98,100,97,90,97)	172.99 (140.43 to 213.09)	144.80 (118.48 to 176.97)	145.42 (117.91 to 179.34)	32.01 (25.75 to 39.79)
Meningitis W(98,100,96,90,97)	260.11 (219.31 to 308.51)	245.63 (208.40 to 289.52)	254.20 (213.76 to 302.30)	193.58 (161.68 to 231.76)
Meningitis Y(N-97,100,97,89,96)	219.52 (173.10 to 278.39)	186.08 (148.25 to 233.55)	204.92 (161.40 to 260.16)	3.66 (2.86 to 4.69)

End point values	MenACWY Group			
Subject group type	Reporting group			
Number of subjects analysed	97			
Units: titers				
geometric mean (confidence interval 80%)				
M14459 (N-97,100,96,90,97)	2.48 (2.13 to 2.89)			
96217 (N-98,100,97,90,96)	4.15 (3.54 to 4.86)			
NZ98/254 (N-98,100,97,89,97)	2.15 (1.81 to 2.57)			
M07-0241084(N-98,100,96,89,95)	4.08 (3.45 to 4.82)			
Meningitis A(N-97,101,97,90,93)	52.03 (43.01 to 62.95)			
Meningitis C (N-98,100,97,90,97)	34.66 (28.09 to 42.78)			
Meningitis W(98,100,96,90,97)	80.11 (67.42 to 95.19)			
Meningitis Y(N-97,100,97,89,96)	92.41 (72.75 to 117.37)			

Statistical analyses

Statistical analysis title	Immune interference-M14459 strain

Statistical analysis description:

Immune interference due to stress to lymph nodes (lymph-node effect) in rMenBOMV+ACWY_S versus rMenBOMV+ACWY_D study groups, on the Meningitis B M14459 (fHbp) strain, one month after last vaccination.

Comparison groups	rMenBOMV+ACWY_S Group v rMenBOMV+ACWY_D Group
Number of subjects included in analysis	198
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Geometric mean ratio
Point estimate	1
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.84
upper limit	1.2

Statistical analysis title	Immune interference- 96217 strain

Statistical analysis description:

Immune interference due to stress to lymph nodes (lymph-node effect) in rMenBOMV+ACWY_S versus rMenBOMV+ACWY_D study groups, on the Meningitis B 96217 (NadA) strain, one month after last vaccination.

Comparison groups	rMenBOMV+ACWY_S Group v rMenBOMV+ACWY_D Group
Number of subjects included in analysis	198
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Geometric mean ratio
Point estimate	1.05
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.88
upper limit	1.26

Statistical analysis title	Immune interference-NZ98/254 strain

Statistical analysis description:

Immune interference due to stress to lymph nodes (lymph-node effect) in rMenBOMV+ACWY_S versus rMenBOMV+ACWY_D study groups, on the Meningitis B NZ98/254 (PorA) strain, one month after last vaccination.

Comparison groups	rMenBOMV+ACWY_S Group v rMenBOMV+ACWY_D Group

Number of subjects included in analysis	198
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Geometric mean ratio
Point estimate	0.78
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.64
upper limit	0.95

Statistical analysis title	Immune interference-M07-0241084 strain

Statistical analysis description:

Immune interference due to stress to lymph nodes (lymph-node effect) in rMenBOMV+ACWY_S versus rMenBOMV+ACWY_D study groups, on the Meningitis B M07-0241084 (NHBA) strain, one month after last vaccination.

Comparison groups	rMenBOMV+ACWY_S Group v rMenBOMV+ACWY_D Group
Number of subjects included in analysis	198
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Geometric mean ratio
Point estimate	0.8
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.66
upper limit	0.96

Statistical analysis title	Immune interference-Serogroup A

Statistical analysis description:

Immune interference due to stress to lymph nodes (lymph-node effect) in rMenBOMV+ACWY_S versus rMenBOMV+ACWY_D study groups, on the Meningitis serogroup A, one month after last vaccination.

Comparison groups	rMenBOMV+ACWY_S Group v rMenBOMV+ACWY_D Group
Number of subjects included in analysis	198
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Geometric mean ratio
Point estimate	0.92
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.74
upper limit	1.14

Statistical analysis title	Immune interference-Serogroup C
Statistical analysis description:	
Immune interference due to stress to lymph nodes (lymph-node effect) in rMenBOMV+ACWY_S versus rMenBOMV+ACWY_D study groups, on the Meningitis serogroup C, one month after last vaccination.	
Comparison groups	rMenBOMV+ACWY_S Group v rMenBOMV+ACWY_D Group
Number of subjects included in analysis	198
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Geometric mean ratio
Point estimate	1
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.78
upper limit	1.27

Statistical analysis title	Immune interference-Serogroup W
Statistical analysis description:	
Immune interference due to stress to lymph nodes (lymph-node effect) in rMenBOMV+ACWY_S versus rMenBOMV+ACWY_D study groups, on the Meningitis serogroup W, one month after last vaccination.	
Comparison groups	rMenBOMV+ACWY_S Group v rMenBOMV+ACWY_D Group
Number of subjects included in analysis	198
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Geometric mean ratio
Point estimate	0.97
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.79
upper limit	1.18

Statistical analysis title	Immune interference-Serogroup Y
Statistical analysis description:	
Immune interference due to stress to lymph nodes (lymph-node effect) in rMenBOMV+ACWY_S versus rMenBOMV+ACWY_D study groups, on the Meningitis serogroup Y, one month after last vaccination.	
Comparison groups	rMenBOMV+ACWY_S Group v rMenBOMV+ACWY_D Group

Number of subjects included in analysis	198
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Geometric mean ratio
Point estimate	0.91
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.69
upper limit	1.19

Statistical analysis title	Other unknown interference-M14459 strain

Statistical analysis description:

Other unknown interference in MenABCWY versus rMenBOMV+ACWY_S study groups, on the Meningitis B M14459 (fHbp) strain, one month after last vaccination.

Comparison groups	MenABCWY Group v rMenBOMV+ACWY_S Group
Number of subjects included in analysis	199
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Geometric mean ratio
Point estimate	1.02
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.86
upper limit	1.22

Statistical analysis title	Other unknown interference-96217 strain

Statistical analysis description:

Other unknown interference in MenABCWY versus rMenBOMV+ACWY_S study groups, on the Meningitis B 96217 (NadA)strain, one month after last vaccination.

Comparison groups	MenABCWY Group v rMenBOMV+ACWY_S Group
Number of subjects included in analysis	199
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Geometric mean ratio
Point estimate	0.79
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.66
upper limit	0.95

Statistical analysis title	Other unknown interference-NZ98/254
Statistical analysis description:	
Other unknown interference in MenABCWY versus rMenBOMV+ACWY_S study groups, on the Meningitis B NZ98/254 (PorA) strain, one month after last vaccination.	
Comparison groups	MenABCWY Group v rMenBOMV+ACWY_S Group
Number of subjects included in analysis	199
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Geometric mean ratio
Point estimate	0.79
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.65
upper limit	0.97

Statistical analysis title	Other unknown interference-M07-0241084
Statistical analysis description:	
Other unknown interference in MenABCWY versus rMenBOMV+ACWY_S study groups, on the Meningitis B M07-0241084 (NHBA) strain, one month after last vaccination.	
Comparison groups	MenABCWY Group v rMenBOMV+ACWY_S Group
Number of subjects included in analysis	199
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Geometric mean ratio
Point estimate	0.73
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.6
upper limit	0.88

Statistical analysis title	Other unknown interference-serogroup A
Statistical analysis description:	
Other unknown interference in MenABCWY versus rMenBOMV+ACWY_S study groups, on the Meningitis serogrpoup A, one month after last vaccination.	
Comparison groups	MenABCWY Group v rMenBOMV+ACWY_S Group

Number of subjects included in analysis	199
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Geometric mean ratio
Point estimate	0.56
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.45
upper limit	0.69

Statistical analysis title	Other unknown interference-Serogroup C

Statistical analysis description:

Other unknown interference in MenABCWY versus rMenBOMV+ACWY_S study groups, on the Meningitis serogroup C, one month after last vaccination.

Comparison groups	MenABCWY Group v rMenBOMV+ACWY_S Group
Number of subjects included in analysis	199
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Geometric mean ratio
Point estimate	1.19
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.94
upper limit	1.52

Statistical analysis title	Other unknown interference-Serogroup W

Statistical analysis description:

Other unknown interference in MenABCWY versus rMenBOMV+ACWY_S study groups, on the Meningitis serogroup W, one month after last vaccination.

Comparison groups	MenABCWY Group v rMenBOMV+ACWY_S Group
Number of subjects included in analysis	199
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Geometric mean ratio
Point estimate	1.06
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.87
upper limit	1.29

Statistical analysis title	Other unknown interference-Serogroup Y

Statistical analysis description:

Other unknown interference in MenABCWY versus rMenBOMV+ACWY_S study groups, on the Meningitis serogroup Y, one month after last vaccination.

Comparison groups	MenABCWY Group v rMenBOMV+ACWY_S Group
Number of subjects included in analysis	199
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Geometric mean ratio
Point estimate	1.18
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.9
upper limit	1.55

Statistical analysis title	Immune response effects-M14459 strain

Statistical analysis description:

To investigate possible effects on the immune response based on strains common to rMenBOMV+ACWY_S versus rMenBOMV study groups, on the Meningitis B M14459(fHbp) strain, one month after last vaccination.

Comparison groups	rMenBOMV+ACWY_S Group v rMenBOMV Group
Number of subjects included in analysis	191
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Geometric mean ratio
Point estimate	1.02
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.85
upper limit	1.22

Statistical analysis title	Immune response effects-96217 strain

Statistical analysis description:

To investigate possible effects on the immune response based on strains common to rMenBOMV+ACWY_S versus rMenBOMV study groups, on the Meningitis B 96217 (NadA) strain, one month after last vaccination.

Comparison groups	rMenBOMV+ACWY_S Group v rMenBOMV Group

Number of subjects included in analysis	191
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Geometric mean ratio
Point estimate	0.9
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.75
upper limit	1.09

Statistical analysis title	Immune response effects-NZ98/254 strain

Statistical analysis description:

To investigate possible effects on the immune response based on strains common to rMenBOMV+ACWY_S versus rMenBOMV study groups, on the Meningitis B NZ98/254 (PorA) strain, one month after last vaccination.

Comparison groups	rMenBOMV+ACWY_S Group v rMenBOMV Group
Number of subjects included in analysis	191
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Geometric mean ratio
Point estimate	0.78
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.64
upper limit	0.96

Statistical analysis title	Immune response effects-M07-0241084 strain

Statistical analysis description:

To investigate possible effects on the immune response based on strains common to rMenBOMV+ACWY_S versus rMenBOMV study groups, on the Meningitis B M07-0241084 (NHBA) strain, one month after last vaccination.

Comparison groups	rMenBOMV+ACWY_S Group v rMenBOMV Group
Number of subjects included in analysis	191
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Geometric mean ratio
Point estimate	0.71
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.58
upper limit	0.86

Statistical analysis title	Immune response effects-Serogroup A
Statistical analysis description: To investigate possible effects on the immune response based on strains common to rMenBOMV+ACWY_S versus MenACWY study groups, on the Meningitis serogroup A, one month after last vaccination.	
Comparison groups	rMenBOMV+ACWY_S Group v MenACWY Group
Number of subjects included in analysis	198
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Geometric mean ratio
Point estimate	3.6
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	2.9
upper limit	4.47

Statistical analysis title	Immune response effects-Serogroup C
Statistical analysis description: To investigate possible effects on the immune response based on strains common to rMenBOMV+ACWY_S versus MenACWY study groups, on the Meningitis serogroup C, one month after last vaccination.	
Comparison groups	rMenBOMV+ACWY_S Group v MenACWY Group
Number of subjects included in analysis	198
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Geometric mean ratio
Point estimate	4.18
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	3.28
upper limit	5.31

Statistical analysis title	Immune response effects-Serogroup W
Statistical analysis description: To investigate possible effects on the immune response based on strains common to rMenBOMV+ACWY_S versus MenACWY study groups, on the Meningitis serogroup W, one month after last vaccination.	
Comparison groups	rMenBOMV+ACWY_S Group v MenACWY Group

Number of subjects included in analysis	198
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Geometric mean ratio
Point estimate	3.07
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	2.52
upper limit	3.73

Statistical analysis title	Immune response effects-Serogroup Y

Statistical analysis description:

To investigate possible effects on the immune response based on strains common to rMenBOMV+ACWY_S versus MenACWY study groups, on the Meningitis serogroup Y, one month after last vaccination.

Comparison groups	rMenBOMV+ACWY_S Group v MenACWY Group
Number of subjects included in analysis	198
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Geometric mean ratio
Point estimate	2.01
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	1.53
upper limit	2.65

Statistical analysis title	Immune response effects-M14459 strain

Statistical analysis description:

To investigate possible effects on the immune response based on strains common to rMenBOMV+ACWY_D versus rMenBOMV study groups, on the Meningitis B M14459 (fHbp) strain, one month after last vaccination.

Comparison groups	rMenBOMV+ACWY_D Group v rMenBOMV Group
Number of subjects included in analysis	187
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Geometric mean ratio
Point estimate	1.02
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.85
upper limit	1.22

Statistical analysis title	Immune response effects-96217 strain

Statistical analysis description:

To investigate possible effects on the immune response based on strains common to rMenBOMV+ACWY_D versus rMenBOMV study groups, on the Meningitis B 96217 (NadA) strain, one month after last vaccination.

Comparison groups	rMenBOMV+ACWY_D Group v rMenBOMV Group
Number of subjects included in analysis	187
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Geometric mean ratio
Point estimate	0.86
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.71
upper limit	1.04

Statistical analysis title	Immune response effects-NZ98/254 strain

Statistical analysis description:

To investigate possible effects on the immune response based on strains common to rMenBOMV+ACWY_D versus rMenBOMV study groups, on the Meningitis B NZ98/254 (PorA) strain, one month after last vaccination.

Comparison groups	rMenBOMV+ACWY_D Group v rMenBOMV Group
Number of subjects included in analysis	187
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Geometric mean ratio
Point estimate	1.01
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.82
upper limit	1.24

Statistical analysis title	Immune response effect-M07-0241084 strain

Statistical analysis description:

To investigate possible effects on the immune response based on strains common to rMenBOMV+ACWY_D versus rMenBOMV study groups, on the Meningitis B M07-0241084 (NHBA) strain, one month after last vaccination.

Comparison groups	rMenBOMV+ACWY_D Group v rMenBOMV Group

Number of subjects included in analysis	187
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Geometric mean ratio
Point estimate	0.89
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.73
upper limit	1.09

Statistical analysis title	Immune response effects- Serogroup A

Statistical analysis description:

To investigate possible effects on the immune response based on strains common to rMenBOMV+ACWY_D versus MenACWY study groups, on the Meningitis serogroup A, one month after last vaccination.

Comparison groups	rMenBOMV+ACWY_D Group v MenACWY Group
Number of subjects included in analysis	194
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Geometric mean ratio
Point estimate	3.92
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	3.15
upper limit	4.88

Statistical analysis title	Immune response effects-Sergroup C

Statistical analysis description:

To investigate possible effects on the immune response based on strains common to rMenBOMV+ACWY_D versus MenACWY study groups, on the Meningitis serogroup C, one month after last vaccination.

Comparison groups	rMenBOMV+ACWY_D Group v MenACWY Group
Number of subjects included in analysis	194
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Geometric mean ratio
Point estimate	4.19
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	3.3
upper limit	5.34

Statistical analysis title	Immune response effects-Serogroup W
Statistical analysis description:	
To investigate possible effects on the immune response based on strains common to rMenBOMV+ACWY_D versus MenACWY study groups, on the Meningitis serogroup W, one month after last vaccination.	
Comparison groups	rMenBOMV+ACWY_D Group v MenACWY Group
Number of subjects included in analysis	194
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Geometric mean ratio
Point estimate	3.17
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	2.6
upper limit	3.87

Statistical analysis title	Immune response effects-Serogroup Y
Statistical analysis description:	
To investigate possible effects on the immune response based on strains common to rMenBOMV+ACWY_D versus MenACWY study groups, on the Meningitis serogroup Y, one month after last vaccination.	
Comparison groups	rMenBOMV+ACWY_D Group v MenACWY Group
Number of subjects included in analysis	194
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Geometric mean ratio
Point estimate	2.22
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	1.68
upper limit	2.92

Statistical analysis title	Immune response effects-M14459 strain
Statistical analysis description:	
To investigate possible effects on the immune response based on strains common to MenABCWY versus rMenBOMV study groups, on the Meningitis B M14459 (fHbp) strain, one month after last vaccination.	
Comparison groups	MenABCWY Group v rMenBOMV Group

Number of subjects included in analysis	188
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Geometric mean ratio
Point estimate	1.05
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.87
upper limit	1.25

Statistical analysis title	Immune response effects-96217 strain

Statistical analysis description:

To investigate possible effects on the immune response based on strains common to MenABCWY versus rMenBOMV study groups, on the Meningitis B 96217 (NadA) strain, one month after last vaccination.

Comparison groups	MenABCWY Group v rMenBOMV Group
Number of subjects included in analysis	188
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Geometric mean ratio
Point estimate	0.71
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.59
upper limit	0.86

Statistical analysis title	Immune response effects-NZ98/254 strain

Statistical analysis description:

To investigate possible effects on the immune response based on strains common to MenABCWY versus rMenBOMV study groups, on the Meningitis B NZ98/254 (PorA) strain, one month after last vaccination.

Comparison groups	MenABCWY Group v rMenBOMV Group
Number of subjects included in analysis	188
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Geometric mean ratio
Point estimate	0.62
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.5
upper limit	0.76

Statistical analysis title	Immune response effects-M07-0241084 strain
Statistical analysis description: To investigate possible effects on the immune response based on strains common to MenABCWY versus rMenBOMV study groups, on the Meningitis B M07-0241084 (NHBA) strain, one month after last vaccination.	
Comparison groups	MenABCWY Group v rMenBOMV Group
Number of subjects included in analysis	188
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Geometric mean ratio
Point estimate	0.52
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.42
upper limit	0.63

Statistical analysis title	Immune response effects-Serogroup A
Statistical analysis description: To investigate possible effects on the immune response based on strains common to MenABCWY versus MenACWY study groups, on the Meningitis serogroup A, one month after last vaccination.	
Comparison groups	MenABCWY Group v MenACWY Group
Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Geometric mean ratio
Point estimate	2.02
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	1.62
upper limit	2.51

Statistical analysis title	Immune response effects-Serogroup C
Statistical analysis description: To investigate possible effects on the immune response based on strains common to MenABCWY versus MenACWY study groups, on the Meningitis serogroup C, one month after last vaccination.	
Comparison groups	MenABCWY Group v MenACWY Group

Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Odds ratio (OR)
Point estimate	4.99
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	3.92
upper limit	6.35

Statistical analysis title	Immune response effects-Serogroup W

Statistical analysis description:

To investigate possible effects on the immune response based on strains common to MenABCWY versus MenACWY study groups, on the Meningitis serogroup W, one month after last vaccination.

Comparison groups	MenABCWY Group v MenACWY Group
Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Geometric mean ratio
Point estimate	3.25
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	2.66
upper limit	3.96

Statistical analysis title	Immune response effects-Serogroup Y

Statistical analysis description:

To investigate possible effects on the immune response based on strains common to MenABCWY versus MenACWY study groups, on the Meningitis serogroup Y, one month after last vaccination.

Comparison groups	MenABCWY Group v MenACWY Group
Number of subjects included in analysis	195
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Geometric mean ratio
Point estimate	2.38
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	1.81
upper limit	3.12

Primary: Percentage of subjects with hSBA titers greater than or equal to(≥) the Lower Limit Of Quantitation (LLOQ) against each of the N. meningitidis serogroup B test strains and serogroups A, C, W-135 and Y,one month after last vaccination.

End point title	Percentage of subjects with hSBA titers greater than or equal to(≥) the Lower Limit Of Quantitation (LLOQ) against each of the N. meningitidis serogroup B test strains and serogroups A, C, W-135 and Y,one month after last vaccination.[2]

End point description:

Immune responses against N. meningitidis serogroup B test strains and N. meningitidis serogroups A, C, W-135, and Y, were calculated in terms of percentage of subjects with hSBA titers ≥ LLOQ. Serogroup B strains tested were M14459 (factor H binding protein; fHbp), 96217 (Neisserial adhesin A; NadA), NZ98/254 (PorA), and M070241084 (Neisseria heparin binding antigen; NHBA). Analysis was performed on PPS for immunogenicity that included subjects who had no major protocol violations and whose assay results were available for at least 1 serogroup or B strain at Day 91 for all study groups except MenACWY Group or at Day 31 for the MenACWY Group.

End point type	Primary

End point timeframe:

1 month after last vaccination i.e.: at Day 91 for all groups except the MenACWY Group, and at Day 31 for the MenACWY Group.

Notes:

[2] - 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: Aim of this endpoint was descriptive analysis. No statistical analyses were performed.

End point values	MenABCWY Group	rMenBOMV+ACWY_S Group	rMenBOMV+ACWY_D Group	rMenBOMV Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	98	101	97	90
Units: Percentage of subjects				
number (confidence interval 80%)				
M14459 (fHbp)(N-97,100,96,90,97)	83.5 (77.64 to 88.28)	86.0 (80.50 to 90.35)	88.5 (83.22 to 92.57)	83.3 (77.18 to 88.31)
96217(NadA)(N-98,100,97,90,96)	96.9 (93.31 to 98.87)	99.0 (96.17 to 99.89)	99.0 (96.05 to 99.89)	100.0 (97.47 to 100.00)
NZ98/254 (PorA)(N-98,100,97,89,97)	59.2 (52.22 to 65.86)	76.0 (69.66 to 81.53)	80.4 (74.27 to 85.57)	78.7 (72.05 to 84.23)
M07-0241084 (NHBA)(N-98,100,96,89,95)	59.2 (52.22 to 65.86)	74.0 (67.54 to 79.71)	77.1 (70.66 to 82.62)	80.9 (74.48 to 86.22)
Meningitis A(N-97,101,97,90,93)	94.8 (90.65 to 97.47)	100.0 (97.75 to 100.00)	99.0 (96.05 to 99.89)	91.1 (85.96 to 94.76)
Meningitis C(N-98,100,97,90,97)	100.0 (97.68 to 100.00)	100.0 (97.72 to 100.00)	100.0 (97.65 to 100.00)	96.7 (92.73 to 98.77)
Meningitis W(N-98,100,96,90,97)	98.0 (94.66 to 99.46)	96.0 (92.17 to 98.24)	99.0 (96.01 to 99.89)	93.3 (88.59 to 96.46)
Menngitis Y(N-97,100,97,89,96)	99.0 (96.05 to 99.89)	98.0 (94.77 to 99.47)	96.9 (93.24 to 98.86)	24.7 (18.79 to 31.54)

End point values	MenACWY Group			
Subject group type	Reporting group			
Number of subjects analysed	97			
Units: Percentage of subjects				

number (confidence interval 80%)				
M14459 (fHbp)(N-97,100,96,90,97)	12.4 (8.21 to 17.78)			
96217(NadA)(N-98,100,97,90,96)	33.3 (26.96 to 40.24)			
NZ98/254 (PorA)(N-98,100,97,89,97)	5.2 (2.53 to 9.35)			
M07-0241084 (NHBA)(N-98,100,96,89,95)	23.2 (17.57 to 29.64)			
Meningitis A(N-97,101,97,90,93)	68.8 (61.86 to 75.15)			
Meningitis C(N-98,100,97,90,97)	86.6 (81.06 to 90.92)			
Meningitis W(N-98,100,96,90,97)	66.0 (59.09 to 72.36)			
Menngitis Y(N-97,100,97,89,96)	85.4 (79.71 to 89.94)			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of subjects with a 4-fold increase in hSBA titers against each of the N. meningitidis serogroup B test strains and against N. meningitidis serogroups A, C, W-135 and Y, one month after last vaccination.

End point title	Percentage of subjects with a 4-fold increase in hSBA titers against each of the N. meningitidis serogroup B test strains and against N. meningitidis serogroups A, C, W-135 and Y, one month after last vaccination.[3]

End point description:

Immune responses against N. meningitidis serogroup B test strains and N. meningitidis serogroups A, C, W-135, and Y, were calculated in terms of percentage of subjects with a 4-fold increase in hSBA titers. A 4-fold rise was defined as: a) for individuals whose pre-vaccination titers were less than (<) the limit of detection (LOD), the post-vaccination titers must have been ≥4-fold the LOD or ≥ the LLOQ, whichever was greater; b) for individuals whose pre-vaccination titers were ≥ the LOD and less than (<) the LLOQ, the post-vaccination titers must have been at least 4 times the LLOQ; and c) for individuals whose pre-vaccination titers were ≥ the LLOQ, the post-vaccination titers must have been at least 4 times the pre-vaccination titer. Serogroup B strains tested were M14459 (factor H binding protein; fHbp), 96217 (Neisserial adhesin A; NadA), NZ98/254 (PorA), and M070241084 (Neisseria heparin binding antigen; NHBA).

End point type	Primary

End point timeframe:

1 month after last vaccination versus baseline (i.e.: at Day 91 versus Day 1 for all groups except the MenACWY Group, and at Day 31 versus Day 1 for the MenACWY Group).

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Aim of this endpoint was descriptive analysis. No statistical analyses were performed.

End point values	MenABCWY Group	rMenBOMV+ACWY_S Group	rMenBOMV+ACWY_D Group	rMenBOMV Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	98	100	97	90
Units: Percentage of subjects				
number (confidence interval 80%)				
M14459 (fHbp)(N-97,100,95,90,97)	66.0 (59.09 to 72.36)	69.0 (62.32 to 75.09)	66.3 (59.36 to 72.74)	63.3 (56.09 to 70.11)

96217(NadA)(N-97,100,95,88,96)	80.4 (74.27 to 85.57)	88.0 (82.74 to 92.04)	90.5 (85.46 to 94.20)	80.7 (74.20 to 86.06)
NZ98/254 (PorA)(N-98,100,97,89,97)	48.0 (41.06 to 54.92)	60.0 (53.11 to 66.58)	58.8 (51.75 to 65.49)	60.7 (53.35 to 67.63)
M07-0241084(NHBA)(N-98,98,95,87,94)	21.4 (16.10 to 27.68)	38.8 (32.18 to 45.72)	42.1 (35.27 to 49.20)	56.3 (48.88 to 63.54)
Meningitis A(96,100,95,90,92)	92.7 (88.04 to 95.90)	99.0 (96.17 to 99.89)	98.9 (95.97 to 99.89)	87.8 (82.14 to 92.06)
Meningitis C(N-98,99,97,89,96)	90.8 (85.89 to 94.38)	91.9 (87.21 to 95.24)	86.6 (81.06 to 90.92)	57.3 (49.95 to 64.40)
Meningitis W(N-96,98,93,85,95)	83.3 (77.41 to 88.15)	78.6 (72.32 to 83.90)	74.2 (67.48 to 80.10)	74.1 (67.04 to 80.30)
Meningitis Y(N-97,99,95,88,95)	95.9 (91.93 to 98.19)	91.9 (87.21 to 95.24)	93.7 (89.18 to 96.65)	11.4 (7.19 to 16.97)

End point values	MenACWY Group			
Subject group type	Reporting group			
Number of subjects analysed	97			
Units: Percentage of subjects				
number (confidence interval 80%)				
M14459 (fHbp)(N-97,100,95,90,97)	2.1 (0.55 to 5.39)			
96217(NadA)(N-97,100,95,88,96)	2.1 (0.56 to 5.45)			
NZ98/254 (PorA)(N-98,100,97,89,97)	1.0 (0.11 to 3.95)			
M07-0241084(NHBA)(N-98,98,95,87,94)	2.1 (0.57 to 5.56)			
Meningitis A(96,100,95,90,92)	67.4 (60.34 to 73.85)			
Meningitis C(N-98,99,97,89,96)	52.1 (45.05 to 59.05)			
Meningitis W(N-96,98,93,85,95)	41.1 (34.26 to 48.14)			
Meningitis Y(N-97,99,95,88,95)	76.8 (70.36 to 82.43)			

Statistical analyses

No statistical analyses for this end point

Primary: hSBA Adjusted Geometric Mean Ratios (GMRs) against each of the N. meningitidis serogroup B test strains and against N. meningitidis serogroups A, C, W-135 and Y, one month after last vaccination.

End point title	hSBA Adjusted Geometric Mean Ratios (GMRs) against each of the N. meningitidis serogroup B test strains and against N. meningitidis serogroups A, C, W-135 and Y, one month after last vaccination.[4]

End point description:

hSBA mean ratios at 1 month after the last vaccination versus baseline were calculated in terms of GMRs i.e. as the anti-logarithm of the mean of the change from baseline of log-transformed titer values at 1 month after last vaccination and Baseline. Serogroup B strains tested were M14459 (factor H binding protein; fHbp), 96217 (Neisserial adhesin A; NadA), NZ98/254 (PorA), and M070241084

(Neisseria heparin binding antigen; NHBA). Adjusted means were obtained from ANCOVA model fitted to each Serogroup (Strain) individually, study group and center as fixed effects and zero-centered pre-vaccination log-transformed titer as a continuous covariate. Analysis was performed on PPS for immunogenicity that included subjects who had no major protocol violations and whose assay results were available for at least 1 serogroup or B strain at Day 91 for all study groups except MenACWY Group or at Day 31 for the MenACWY Group and at baseline for all study groups.

End point type	Primary

End point timeframe:

1 month after last vaccination versus baseline (i.e.: at Day 91 versus Day 1 for all groups except the MenACWY Group, and at Day 31 versus Day 1 for the MenACWY Group).

Notes:

[4] - 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: Aim of this endpoint was descriptive analysis. No statistical analyses were performed.

End point values	MenABCWY Group	rMenBOMV+ACWY_S Group	rMenBOMV+ACWY_D Group	rMenBOMV Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	98	100	97	90
Units: Ratio				
geometric mean (confidence interval 80%)				
M14459(N-97,100,95,90,97)	11.17 (9.59 to 13.02)	10.90 (9.42 to 12.62)	10.85 (9.30 to 12.66)	10.69 (9.12 to 12.52)
96217(N-97,100,95,88,96)	21.33 (18.22 to 24.99)	27.02 (23.22 to 31.44)	25.66 (21.88 to 30.10)	29.87 (25.32 to 35.24)
NZ98/254(N-98,100,97,89,97)	7.28 (6.11 to 8.67)	9.20 (7.78 to 10.88)	11.85 (9.94 to 14.13)	11.77 (9.81 to 14.12)
M07-0241084(NHBA)(N-98,98,95,87,94)	3.60 (3.05 to 4.25)	4.96 (4.23 to 5.81)	6.22 (5.27 to 7.35)	6.98 (5.87 to 8.30)
Meningitis A(N-96,100,95,90,92)	33.21 (27.55 to 40.04)	59.36 (49.68 to 70.93)	64.58 (53.52 to 77.93)	30.05 (24.77 to 36.44)
Meningitis C(N-98,99,97,89,96)	34.34 (27.88 to 42.30)	28.74 (23.52 to 35.13)	28.86 (23.40 to 35.60)	6.35 (5.11 to 7.90)
Meningitis W(N-96,98,93,85,95)	24.58 (20.72 to 29.15)	23.21 (19.69 to 27.36)	24.02 (20.20 to 28.56)	18.29 (15.28 to 21.90)
Meningitis Y(N-97,99,95,88,95)	106.87 (84.27 to 135.53)	90.59 (72.18 to 113.70)	99.76 (78.58 to 126.66)	1.78 (1.39 to 2.28)

End point values	MenACWY Group			
Subject group type	Reporting group			
Number of subjects analysed	97			
Units: Ratio				
geometric mean (confidence interval 80%)				
M14459(N-97,100,95,90,97)	1.16 (0.99 to 1.35)			
96217(N-97,100,95,88,96)	1.09 (0.93 to 1.28)			
NZ98/254(N-98,100,97,89,97)	1.21 (1.01 to 1.44)			
M07-0241084(NHBA)(N-98,98,95,87,94)	1.12 (0.95 to 1.33)			
Meningitis A(N-96,100,95,90,92)	16.47 (13.62 to 19.93)			

Meningitis C(N-98,99,97,89,96)	6.88 (5.58 to 8.49)			
Meningitis W(N-96,98,93,85,95)	7.57 (6.37 to 8.99)			
Meningitis Y(N-97,99,95,88,95)	44.99 (35.42 to 57.14)			

Statistical analyses

No statistical analyses for this end point

Secondary: hSBA Adjusted GMTs against all of N. meningitidis serogroup B test strains (pooled), one month after first vaccination

End point title	hSBA Adjusted GMTs against all of N. meningitidis serogroup B test strains (pooled), one month after first vaccination[5]

End point description:

hSBA titers against all of N. meningitidis serogroup B test strains were calculated in terms of GMTs. Serogroup B strains tested were M14459 (factor H binding protein; fHbp), 96217 (Neisserial adhesin A; NadA), NZ98/254 (PorA), and M070241084 (Neisseria heparin binding antigen; NHBA). The serogroup B strains were grouped together to perform a pooled analysis. Adjusted means were obtained from ANCOVA model fitted to all of the Serogroup B test strains, study group, test strain and center as fixed effects; zero-centered pre-vaccination log-transformed titer was included as a continuous covariate. Analysis was performed on PPS for immunogenicity that included subjects who had no major protocol violations and whose assay results were available for at least 1 serogroup or B strain after first vaccination for all study groups except for MenACWY group that was not considered for this analysis as only serogroup B strains assessed in this outcome.

End point type	Secondary

End point timeframe:

1 month after first vaccination i.e.: at Day 31 for all groups except for the MenACWY Group

Notes:

[5] - 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: MenACWY group was not considered for this analysis as only serogroup B strains were assessed in this outcome measure.

End point values	MenABCWY Group	rMenBOMV+ACWY_S Group	rMenBOMV+ACWY_D Group	rMenBOMV Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	96	103	98	91
Units: Titers				
geometric mean (confidence interval 80%)	6.51 (5.63 to 7.52)	8.33 (7.24 to 9.58)	8.16 (7.08 to 9.41)	9.45 (8.14 to 10.95)

Statistical analyses

Statistical analysis title	Immune interference- Pooled B strains

Statistical analysis description:

Immune interference due to stress to lymph nodes (lymph-node effect) in rMenBOMV+ACWY_S versus rMenBOMV+ACWY_D study groups, on the pooled B strains, one month after first vaccination.

Comparison groups	rMenBOMV+ACWY_S Group v rMenBOMV+ACWY_D Group

Number of subjects included in analysis	201
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Geometric mean ratio
Point estimate	1.02
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.86
upper limit	1.22

Secondary: hSBA Adjusted GMTs against each of the N. meningitidis serogroup B test strains and N. meningitidis serogroups A, C, W-135 and Y, one month after first vaccination.

End point title	hSBA Adjusted GMTs against each of the N. meningitidis serogroup B test strains and N. meningitidis serogroups A, C, W-135 and Y, one month after first vaccination.[6]

End point description:

hSBA titers against each of the N. meningitidis serogroup B test strains and N. meningitidis serogroups A, C, W-135, and Y were calculated in terms of GMTs. Serogroup B strains tested were M14459 (factor H binding protein; fHbp), 96217 (Neisserial adhesin A; NadA), NZ98/254 (PorA), and M070241084 (Neisseria heparin binding antigen; NHBA). Adjusted means were obtained from ANCOVA model fitted to each Serogroup (Strain) individually, study group and center as fixed effects and zero-centered pre-vaccination log-transformed titer as a continuous covariate. Analysis was performed on PPS for immunogenicity that included subjects who had no major protocol violations and whose assay results were available for at least 1 serogroup or B strain after first vaccination for all study groups except for MenACWY Group for which results were included in the last vaccination analysis (see primary outcome measure 2).

End point type	Secondary

End point timeframe:

1 month after first vaccination i.e.: at Day 31 for all groups except for the MenACWY Group.

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: MenACWY group was not considered for this analysis as only serogroup B strains were assessed in this outcome measure.

End point values	MenABCWY Group	rMenBOMV+ACWY_S Group	rMenBOMV+ACWY_D Group	rMenBOMV Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	96	103	98	91
Units: Titers				
geometric mean (confidence interval 80%)				
M14459 (N-95,103,98,90)	5.50 (4.55 to 6.66)	6.36 (5.29 to 7.65)	4.94 (4.09 to 5.96)	6.08 (5.00 to 7.39)
96217	8.21 (6.87 to 9.81)	11.30 (9.51 to 13.42)	12.18 (10.23 to 14.52)	14.07 (11.72 to 16.89)
NZ98/254 (N-96,103,98,90)	3.79 (3.10 to 4.63)	4.83 (3.98 to 5.86)	4.76 (3.91 to 5.79)	5.48 (4.47 to 6.71)
M07-0241084(N-94,101,96,90)	6.27 (5.23 to 7.52)	7.31 (6.12 to 8.73)	6.75 (5.65 to 8.06)	7.69 (6.38 to 9.26)
Meningitis A(N-95,102,96,90)	31.38 (24.79 to 39.73)	67.95 (54.07 to 85.40)	88.29 (69.95 to 111.44)	8.22 (6.48 to 10.44)

Meningitis C(N-96,102,97,90)	41.35 (32.39 to 52.79)	33.76 (26.61 to 42.85)	40.33 (31.71 to 51.29)	11.47 (8.92 to 14.74)
Meningitis W(N-96,102,97,88)	108.91 (88.67 to 133.78)	81.38 (66.62 to 99.42)	92.84 (75.75 to 113.80)	42.99 (34.66 to 53.33)
Meningitis Y(N-95,99,95,90)	75.07 (56.86 to 99.13)	76.48 (58.31 to 100.32)	100.30 (76.13 to 132.15)	3.98 (3.00 to 5.30)

Statistical analyses

Statistical analysis title	Immune interference-M14459 strain

Statistical analysis description:

Immune interference due to stress to lymph nodes (lymph-node effect) in rMenBOMV+ACWY_S versus rMenBOMV+ACWY_D study groups, on the Meningitis B M14459 (fHbp) strain, one month after first vaccination.

Comparison groups	rMenBOMV+ACWY_S Group v rMenBOMV+ACWY_D Group
Number of subjects included in analysis	201
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Geometric mean ratio
Point estimate	1.29
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	1.02
upper limit	1.63

Statistical analysis title	Immune interference-96217 strain

Statistical analysis description:

Immune interference due to stress to lymph nodes (lymph-node effect) in rMenBOMV+ACWY_S versus rMenBOMV+ACWY_D study groups, on the Meningitis B 96217 (NadA) strain, one month after first vaccination.

Comparison groups	rMenBOMV+ACWY_S Group v rMenBOMV+ACWY_D Group
Number of subjects included in analysis	201
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Geometric mean ratio
Point estimate	0.93
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.75
upper limit	1.15

Statistical analysis title	Immune interference-NZ98/254 strain

Statistical analysis description:

Immune interference due to stress to lymph nodes (lymph-node effect) in rMenBOMV+ACWY_S versus rMenBOMV+ACWY_D study groups, on the Meningitis B NZ98/254 (PorA)strain, one month after first vaccination.

Comparison groups	rMenBOMV+ACWY_S Group v rMenBOMV+ACWY_D Group
Number of subjects included in analysis	201
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Geometric mean ratio
Point estimate	1.01
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.8
upper limit	1.29

Statistical analysis title	Immune interference-M07-0241084 strain

Statistical analysis description:

Immune interference due to stress to lymph nodes (lymph-node effect) in rMenBOMV+ACWY_S versus rMenBOMV+ACWY_D study groups, on the Meningitis B M07-0241084 (NHBA) strain, one month after first vaccination.

Comparison groups	rMenBOMV+ACWY_S Group v rMenBOMV+ACWY_D Group
Number of subjects included in analysis	201
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Odds ratio (OR)
Point estimate	1.08
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.87
upper limit	1.36

Statistical analysis title	Immune interference-Serogroup A

Statistical analysis description:

Immune interference due to stress to lymph nodes (lymph-node effect) in rMenBOMV+ACWY_S versus rMenBOMV+ACWY_D study groups, on the Meningitis serogroup A, one month after first vaccination.

Comparison groups	rMenBOMV+ACWY_S Group v rMenBOMV+ACWY_D Group
Number of subjects included in analysis	201
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Geometric mean ratio
Point estimate	0.77

Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.58
upper limit	1.03

Statistical analysis title	Immune interference-Serogroup C
Statistical analysis description:	
Immune interference due to stress to lymph nodes (lymph-node effect) in rMenBOMV+ACWY_S versus rMenBOMV+ACWY_D study groups, on the Meningitis serogroup C, one month after first vaccination.	
Comparison groups	rMenBOMV+ACWY_S Group v rMenBOMV+ACWY_D Group
Number of subjects included in analysis	201
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Geometric mean ratio
Point estimate	0.84
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.62
upper limit	1.13

Statistical analysis title	Immune interference-Serogroup W
Statistical analysis description:	
Immune interference due to stress to lymph nodes (lymph-node effect) in rMenBOMV+ACWY_S versus rMenBOMV+ACWY_D study groups, on the Meningitis serogroup W, one month after first vaccination.	
Comparison groups	rMenBOMV+ACWY_S Group v rMenBOMV+ACWY_D Group
Number of subjects included in analysis	201
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Geometric mean ratio
Point estimate	0.88
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.68
upper limit	1.13

Statistical analysis title	Immune interference-Serogroup Y
Statistical analysis description:	
Immune interference due to stress to lymph nodes (lymph-node effect) in rMenBOMV+ACWY_S versus rMenBOMV+ACWY_D study groups, on the Meningitis serogroup Y, one month after first vaccination.	
Comparison groups	rMenBOMV+ACWY_S Group v rMenBOMV+ACWY_D Group

Number of subjects included in analysis	201
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Geometric mean ratio
Point estimate	0.76
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.54
upper limit	1.08

Statistical analysis title	Other unknown interference-M14459 strain

Statistical analysis description:

Other unknown interference in MenABCWY versus rMenBOMV+ACWY_S study groups, on the Meningitis B M14459 (fHbp) strain, one month after first vaccination.

Comparison groups	MenABCWY Group v rMenBOMV+ACWY_S Group
Number of subjects included in analysis	199
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Geometric mean ratio
Point estimate	0.87
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.69
upper limit	1.09

Statistical analysis title	Other unknown interference-96217 strain

Statistical analysis description:

Other unknown interference in MenABCWY versus rMenBOMV+ACWY_S study groups, on the Meningitis B 96217 (NadA) strain, one month after first vaccination.

Comparison groups	MenABCWY Group v rMenBOMV+ACWY_S Group
Number of subjects included in analysis	199
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Geometric mean ratio
Point estimate	0.73
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.58
upper limit	0.9

Statistical analysis title	Other unknown interference-NZ98/254 strain
Statistical analysis description:	
Other unknown interference in MenABCWY versus rMenBOMV+ACWY_S study groups, on the Meningitis B NZ98/254 (PorA) strain, one month after first vaccination.	
Comparison groups	MenABCWY Group v rMenBOMV+ACWY_S Group
Number of subjects included in analysis	199
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Geometric mean ratio
Point estimate	0.78
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.61
upper limit	1

Statistical analysis title	Other unknown interference-M07-0241084
Statistical analysis description:	
Other unknown interference in MenABCWY versus rMenBOMV+ACWY_S study groups, on the Meningitis B M07-0241084 (NHBA) strain, one month after first vaccination.	
Comparison groups	MenABCWY Group v rMenBOMV+ACWY_S Group
Number of subjects included in analysis	199
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Geometric mean ratio
Point estimate	0.86
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.68
upper limit	1.07

Statistical analysis title	Other unknown interference-Serogroup A
Statistical analysis description:	
Other unknown interference in MenABCWY versus rMenBOMV+ACWY_S study groups, on the Meningitis serogroup A, one month after first vaccination.	
Comparison groups	MenABCWY Group v rMenBOMV+ACWY_S Group

Number of subjects included in analysis	199
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Geometric mean ratio
Point estimate	0.46
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.35
upper limit	0.62

Statistical analysis title	Other unknown interference-Serogroup C

Statistical analysis description:

Other unknown interference in MenABCWY versus rMenBOMV+ACWY_S study groups, on the Meningitis serogroup C, one month after first vaccination.

Comparison groups	MenABCWY Group v rMenBOMV+ACWY_S Group
Number of subjects included in analysis	199
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Geometric mean ratio
Point estimate	1.22
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.91
upper limit	1.65

Statistical analysis title	Other unknown interference-Serogroup W

Statistical analysis description:

Other unknown interference in MenABCWY versus rMenBOMV+ACWY_S study groups, on the Meningitis serogroup W, one month after first vaccination.

Comparison groups	MenABCWY Group v rMenBOMV+ACWY_S Group
Number of subjects included in analysis	199
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Geometric mean ratio
Point estimate	1.34
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	1.04
upper limit	1.72

Statistical analysis title	Other unknown interference-Serogroup Y

Statistical analysis description:

Other unknown interference in MenABCWY versus rMenBOMV+ACWY_S study groups, on the Meningitis serogroup Y, one month after first vaccination.

Comparison groups	MenABCWY Group v rMenBOMV+ACWY_S Group
Number of subjects included in analysis	199
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Geometric mean ratio
Point estimate	0.98
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.7
upper limit	1.38

Statistical analysis title	Immune response effects-M14459 strain

Statistical analysis description:

To investigate possible effects on the immune response based on strains common to rMenBOMV+ACWY_S versus rMenBOMV study groups, on the Meningitis B M14459 (fHbp) strain, one month after first vaccination.

Comparison groups	rMenBOMV+ACWY_S Group v rMenBOMV Group
Number of subjects included in analysis	194
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Geometric mean ratio
Point estimate	1.05
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.83
upper limit	1.32

Statistical analysis title	Immune response effects-96217 strain

Statistical analysis description:

To investigate possible effects on the immune response based on strains common to rMenBOMV+ACWY_S versus rMenBOMV study groups, on the Meningitis B 96217 (NadA) strain, one month after first vaccination.

Comparison groups	rMenBOMV+ACWY_S Group v rMenBOMV Group

Number of subjects included in analysis	194
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Geometric mean ratio
Point estimate	0.8
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.64
upper limit	1

Statistical analysis title	Immune response effects-NZ98/254 strain

Statistical analysis description:

To investigate possible effects on the immune response based on strains common to rMenBOMV+ACWY_S versus rMenBOMV study groups, on the Meningitis B NZ98/254 (PorA) strain, one month after first vaccination.

Comparison groups	rMenBOMV+ACWY_S Group v rMenBOMV Group
Number of subjects included in analysis	194
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Geometric mean ratio
Point estimate	0.88
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.69
upper limit	1.13

Statistical analysis title	Immune response effects-M07-0241084

Statistical analysis description:

To investigate possible effects on the immune response based on strains common to rMenBOMV+ACWY_S versus rMenBOMV study groups, on the Meningitis B M07-0241084 (NHBA) strain, one month after first vaccination.

Comparison groups	rMenBOMV+ACWY_S Group v rMenBOMV Group
Number of subjects included in analysis	194
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Geometric mean ratio
Point estimate	0.95
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.76
upper limit	1.19

Statistical analysis title	Immune response effects- M14459 strain

Statistical analysis description:

To investigate possible effects on the immune response based on strains common to rMenBOMV+ACWY_D versus rMenBOMV study groups, on the Meningitis B M14459 (fHbp) strain, one month after first vaccination.

Comparison groups	rMenBOMV+ACWY_D Group v rMenBOMV Group
Number of subjects included in analysis	189
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Geometric mean ratio
Point estimate	0.81
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.64
upper limit	1.03

Statistical analysis title	Immune response effects- 96217 strain

Statistical analysis description:

To investigate possible effects on the immune response based on strains common to rMenBOMV+ACWY_D versus rMenBOMV study groups, on the Meningitis B 96217 (NadA) strain, one month after first vaccination.

Comparison groups	rMenBOMV+ACWY_D Group v rMenBOMV Group
Number of subjects included in analysis	189
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Geometric mean ratio
Point estimate	0.87
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.69
upper limit	1.09

Statistical analysis title	Immune response effects-NZ98/254 strain

Statistical analysis description:

To investigate possible effects on the immune response based on strains common to rMenBOMV+ACWY_D versus rMenBOMV study groups, on the Meningitis B NZ98/254 (PorA) strain, one month after first vaccination.

Comparison groups	rMenBOMV+ACWY_D Group v rMenBOMV Group

Number of subjects included in analysis	189
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Geometrical mean ratio
Point estimate	0.87
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.68
upper limit	1.12

Statistical analysis title	Immune response effects-M07-0241084

Statistical analysis description:

To investigate possible effects on the immune response based on strains common to rMenBOMV+ACWY_D versus rMenBOMV study groups, on the Meningitis B M07-0241084 (NHBA) strain, one month after first vaccination.

Comparison groups	rMenBOMV+ACWY_D Group v rMenBOMV Group
Number of subjects included in analysis	189
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Geometrical mean ratio
Point estimate	0.88
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.7
upper limit	1.1

Statistical analysis title	Immune response effects-M14459 strain

Statistical analysis description:

To investigate possible effects on the immune response based on strains common to MenABCWY versus rMenBOMV study groups, on the Meningitis B M14459 (fHbp)strain, one month after first vaccination.

Comparison groups	MenABCWY Group v rMenBOMV Group
Number of subjects included in analysis	187
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Geometric mean ratio
Point estimate	0.91
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.71
upper limit	1.15

Statistical analysis title	Immune response effects-96217 strain
Statistical analysis description:	
To investigate possible effects on the immune response based on strains common to MenABCWY versus rMenBOMV study groups, on the Meningitis B 96217 (NadA) strain, one month after first vaccination.	
Comparison groups	MenABCWY Group v rMenBOMV Group
Number of subjects included in analysis	187
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Geometric mean ratio
Point estimate	0.58
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.47
upper limit	0.73

Statistical analysis title	Immune response effects-NZ98/254 strain
Statistical analysis description:	
To investigate possible effects on the immune response based on strains common to MenABCWY versus rMenBOMV study groups, on the Meningitis B NZ98/254 (PorA) strain, one month after first vaccination.	
Comparison groups	MenABCWY Group v rMenBOMV Group
Number of subjects included in analysis	187
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Geometric mean ratio
Point estimate	0.69
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.54
upper limit	0.89

Statistical analysis title	Immune response effects-M07-0241084
Statistical analysis description:	
To investigate possible effects on the immune response based on strains common to MenABCWY versus rMenBOMV study groups, on the Meningitis B M07-0241084 (NHBA) strain, one month after first vaccination.	
Comparison groups	MenABCWY Group v rMenBOMV Group

Number of subjects included in analysis	187
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	Geometric mean ratio
Point estimate	0.82
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.65
upper limit	1.03

Secondary: Percentage of subjects with hSBA titers greater than or equal to (≥) the LLOQ against each of the N. meningitidis serogroup B test strains and against serogroups A, C, W-135, and Y, one month after first vaccination

End point title	Percentage of subjects with hSBA titers greater than or equal to (≥) the LLOQ against each of the N. meningitidis serogroup B test strains and against serogroups A, C, W-135, and Y, one month after first vaccination[7]

End point description:

Immune responses against N. meningitidis serogroup B test strains and N. meningitidis serogroups A, C, W-135, and Y, were calculated in terms of percentage of subjects with hSBA titers ≥ LLOQ. Serogroup B strains tested were M14459 (factor H binding protein; fHbp), 96217 (Neisserial adhesin A; NadA), NZ98/254 (PorA), and M070241084 (Neisseria heparin binding antigen; NHBA). Analysis was performed on PPS for immunogenicity that included subjects who had no major protocol violations and whose assay results were available for at least 1 serogroup or B strain after first vaccination for all study groups except for MenACWY Group for which results were included in the last vaccination analysis (see primary outcome measure 3).

End point type	Secondary

End point timeframe:

1 month after first vaccination i.e.: at Day 31 for all groups except for the MenACWY Group

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: MenACWY group was not considered for this analysis as only serogroup B strains were assessed in this outcome measure.

End point values	MenABCWY Group	rMenBOMV+ACWY_S Group	rMenBOMV+ACWY_D Group	rMenBOMV Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	96	103	98	91
Units: Percentage of subjects				
number (confidence interval 80%)				
M14459 (fHbp)(N-95,103,98,90)	36.8 (30.24 to 43.88)	49.5 (42.77 to 56.27)	37.8 (31.21 to 44.69)	42.2 (35.19 to 49.53)
96217 (NadA)	57.3 (50.24 to 64.11)	66.0 (59.35 to 72.20)	69.4 (62.65 to 75.51)	75.8 (69.12 to 81.64)
NZ98/254 (PorA)(N-96,103,98,90)	29.2 (23.08 to 35.93)	37.9 (31.48 to 44.61)	33.7 (27.35 to 40.51)	37.8 (30.94 to 45.04)
M07-0241084 (NHBA)(N-94,101,96,90)	35.1 (28.56 to 42.14)	49.5 (42.69 to 56.33)	37.5 (30.90 to 44.51)	44.4 (37.33 to 51.75)
Meningitis A(N-95,102,97,90)	65.3 (58.28 to 71.75)	73.5 (67.12 to 79.22)	80.2 (74.01 to 85.41)	25.6 (19.58 to 32.38)
Meningitis C(N-96,102,97,90)	89.6 (84.41 to 93.42)	94.1 (89.90 to 96.88)	92.8 (88.16 to 95.94)	70.0 (62.96 to 76.35)

Meningitis W(N-96,102,97,88)	71.9 (65.16 to 77.88)	70.6 (64.04 to 76.51)	74.2 (67.67 to 80.00)	52.3 (44.90 to 59.56)
Meningitis Y(N-95,99,95,90)	83.2 (77.18 to 88.02)	81.8 (75.86 to 86.76)	88.4 (83.05 to 92.49)	20.0 (14.60 to 26.45)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with a 4-fold increase in hSBA titers against each of the N. meningitidis serogroup B test strains and against N. meningitidis serogroups A, C, W-135, and Y, one month after first vaccination

End point title	Percentage of subjects with a 4-fold increase in hSBA titers against each of the N. meningitidis serogroup B test strains and against N. meningitidis serogroups A, C, W-135, and Y, one month after first vaccination[8]

End point description:

Immune responses against N. meningitidis serogroup B test strains and N. meningitidis serogroups A, C, W-135, and Y, were calculated in terms of percentage of subjects with a 4-fold increase in hSBA titers. A 4-fold rise is defined as: a) for individuals whose pre-vaccination titers were less than (<) the limit of detection (LOD), the post-vaccination titers must have been ≥4-fold the LOD or ≥ the LLOQ, whichever was greater; b) for individuals whose pre-vaccination titers were ≥ the LOD and less than (<) the LLOQ, the post-vaccination titers must have been at least 4 times the LLOQ; and c) for individuals whose pre-vaccination titers were ≥ the LLOQ, the post-vaccination titers must have been at least 4 times the pre-vaccination titer. Serogroup B strains tested were M14459 (factor H binding protein; fHbp), 96217 (Neisserial adhesin A; NadA), NZ98/254 (PorA), and M070241084 (Neisseria heparin binding antigen; NHBA).

End point type	Secondary

End point timeframe:

1 month after first vaccination versus baseline (i.e.: at Day 31 versus Day 1 for all groups except for the MenACWY Group)

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: MenACWY group was not considered for this analysis as only serogroup B strains were assessed in this outcome measure.

End point values	MenABCWY Group	rMenBOMV+ACWY_S Group	rMenBOMV+ACWY_D Group	rMenBOMV Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	96	103	97	91
Units: Percentage of subjects				
number (confidence interval 80%)				
M14459 (fHbp)(N-95,103,96,90)	24.2 (18.52 to 30.76)	24.3 (18.80 to 30.53)	18.8 (13.67 to 24.86)	25.6 (19.58 to 32.38)
96217 (NadA)(N-95,103,95,89)	22.1 (16.62 to 28.51)	34.0 (27.80 to 40.65)	30.5 (24.31 to 37.38)	32.6 (26.01 to 39.77)
NZ98/254 (PorA)(N-96,103,97,90)	20.8 (15.51 to 27.11)	26.2 (20.57 to 32.58)	26.8 (20.94 to 33.42)	27.8 (21.60 to 34.72)
M07-0241084 (NHBA)(N-94,97,94,88)	9.6 (5.86 to 14.69)	20.6 (15.35 to 26.84)	13.8 (9.37 to 19.52)	20.5 (14.94 to 27.03)
Meningitis A(N-94,101,93,90)	61.7 (54.60 to 68.42)	71.3 (64.73 to 77.18)	80.6 (74.37 to 85.88)	23.3 (17.57 to 30.03)
Meningitis C(N-96,101,96,89)	54.2 (47.11 to 61.09)	46.5 (39.78 to 53.39)	51.0 (44.02 to 58.03)	24.7 (18.79 to 31.54)
Meningitis W(N-94,100,93,83)	60.6 (53.53 to 67.40)	52.0 (45.12 to 58.82)	51.6 (44.46 to 58.71)	39.8 (32.53 to 47.37)

Meningitis Y(N-95,98,92,89)	77.9 (71.49 to 83.38)	75.5 (69.06 to 81.14)	78.3 (71.76 to 83.79)	9.0 (5.30 to 14.19)

Statistical analyses

No statistical analyses for this end point

Secondary: hSBA Adjusted GMRs against each of the N. meningitidis serogroup B test strains and against N. meningitidis serogroups A, C, W-135, and Y, one month after first vaccination

End point title	hSBA Adjusted GMRs against each of the N. meningitidis serogroup B test strains and against N. meningitidis serogroups A, C, W-135, and Y, one month after first vaccination[9]

End point description:

hSBA mean ratios at 1 month after the first vaccination versus baseline were calculated in terms of GMRs i.e. as the anti-logarithm of the mean of the change from baseline of log-transformed titer values at 1 month after last vaccination and Baseline. Serogroup B strains tested were M14459 (factor H binding protein; fHbp),96217 (Neisserial adhesin A; NadA),NZ98/254 (PorA) and M070241084 (Neisseria heparin binding antigen; NHBA).Adjusted mean was obtained from ANCOVA model fitted to each Serogroup (Strain) individually,study group and center as fixed effects and zero-centered pre-vaccination log-transformed titer as a continuous covariate.Analysis was performed on PPS for immunogenicity that included subjects who had no major protocol violations and whose assay results were available for at least 1 serogroup or B strain after first vaccination for all study groups except for MenACWY Group for which results were included in the last vaccination analysis (see primary outcome measure 5)

End point type	Secondary

End point timeframe:

1 month after first vaccination versus baseline (i.e.: at Day 31 versus Day 1 for all groups except for the MenACWY Group)

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: MenACWY group was not considered for this analysis as only serogroup B strains were assessed in this outcome measure.

End point values	MenABCWY Group	rMenBOMV+ACWY_S Group	rMenBOMV+ACWY_D Group	rMenBOMV Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	96	103	97	90
Units: Ratio				
geometric mean (confidence interval 80%)				
M14459 (N-95,103,96,90)	2.59 (2.14 to 3.14)	3.00 (2.49 to 3.61)	2.33 (1.93 to 2.81)	2.87 (2.36 to 3.48)
96217(N-95,103,95,89)	2.15 (1.80 to 2.57)	2.96 (2.49 to 3.51)	3.19 (2.68 to 3.80)	3.68 (3.07 to 4.42)
NZ98/254 (N-96,103,97,90)	2.16 (1.77 to 2.64)	2.76 (2.27 to 3.34)	2.72 (2.23 to 3.31)	3.13 (2.55 to 3.83)
M07-0241084 (N-94,97,94,88)	1.73 (1.44 to 2.07)	2.01 (1.69 to 2.41)	1.86 (1.56 to 2.22)	2.12 (1.76 to 2.55)
Meningitis A(N-94,101,93,90)	10.15 (8.02 to 12.85)	21.97 (17.48 to 27.62)	28.55 (22.62 to 36.04)	2.66 (2.09 to 3.38)
Meningitis C(N-96,101,96,89)	8.08 (6.33 to 10.31)	6.59 (5.20 to 8.37)	7.88 (6.19 to 10.02)	2.24 (1.74 to 2.88)
Meningitis W(N-94,100,93,83)	11.08 (9.02 to 13.60)	8.28 (6.77 to 10.11)	9.44 (7.70 to 11.57)	4.37 (3.52 to 5.42)

Meningitis Y(N-95,98,92,89)	36.58 (27.70 to 48.30)	37.26 (28.41 to 48.88)	48.87 (37.09 to 64.39)	1.94 (1.46 to 2.58)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any solicited local Adverse Events (AEs)

End point title	Number of subjects with any solicited local Adverse Events (AEs)

End point description:

Assessed local AEs were erythema, swelling, induration and pain. Any erythema, swelling and induration is defined as a symptom with a surface diameter equal to or greater than 25 millimeters.Analysis was performed on the solicited safety set that included all subjects who provided informed consent, underwent screening procedures, had a subject number assigned, received a study vaccination and was reported with any solicited adverse event data. No results for dose 2 categories for subjects of MenACWY Group as they received only 1 dose at day 1.

End point type	Secondary

End point timeframe:

During the 7 days (including the day of vaccination) after each vaccination i.e after Dose 1 administered at Day 1 (for all groups) and after Dose 2 administered at Day 61 (for all groups except for MenACWY Group)

End point values	MenABCWY Group	rMenBOMV+ACWY_S Group	rMenBOMV+ACWY_D Group	rMenBOMV Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	100	104	100	94
Units: Participants				
Erythema at Dose 1	17	19	18	9
Swelling at Dose 1	20	21	16	13
Induration at Dose 1	9	15	12	6
Pain at Dose 1	89	100	95	88
Erythema at Dose 2	15	18	15	10
Swelling at Dose 2	13	14	15	12
Induration at Dose 2	6	11	12	12
Pain at Dose 2	87	97	95	87

End point values	MenACWY Group			
Subject group type	Reporting group			
Number of subjects analysed	102			
Units: Participants				
Erythema at Dose 1	7			
Swelling at Dose 1	10			
Induration at Dose 1	4			
Pain at Dose 1	52			

Erythema at Dose 2	0			
Swelling at Dose 2	0			
Induration at Dose 2	0			
Pain at Dose 2	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any solicited systemic AEs

End point title	Number of subjects with any solicited systemic AEs

End point description:

Assessed systemic AEs were arthralgia, fatigue, nausea, headache, myalgia and fever. Any fever is defined as body temperature equal or greater than 38 degrees Celsius. Analysis was performed on the solicited safety set that included all subjects who provided informed consent, underwent screening procedures, had a subject number assigned, received a study vaccination and was reported with any solicited adverse event data. No results for dose 2 category for subjects of MenACWY Group as they received only 1 dose at day 1.

End point type	Secondary

End point timeframe:

During the 7 days (including the day of vaccination) after each vaccination i.e after Dose 1 administered at Day 1 (for all groups) and after Dose 2 administered at Day 61 (for all groups except for MenACWY Group)

End point values	MenABCWY Group	rMenBOMV+ACWY_S Group	rMenBOMV+ACWY_D Group	rMenBOMV Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	100	104	100	94
Units: Participants				
Arthralgia at Dose 1(N-98,100,96,86,98)	20	15	9	9
Fatigue at Dose 1(N-99,102,100,92,100)	56	61	55	46
Nausea at Dose 1(N-97,101,97,85,99)	16	23	14	13
Headache at Dose 1(98,102,98,92,99)	40	46	38	36
Myalgia at Dose 1(N-98,101,97,87,99)	34	29	27	21
Fever at Dose 1(N-100,103,100,94,101)	6	5	5	1
Arthralgia at Dose 2(N-98,103,98,92,0)	22	19	12	17
Fatigue at Dose 2(N-100,104,100,94,0)	58	61	62	56
Nausea at Dose 2(N-98,102,98,93,0)	16	13	15	17
Headache at Dose 2(N-98,104,100,93,0)	52	36	37	39
Myalgia at Dose 2(N-98,103,99,94,0)	41	38	35	38
Fever at Dose 2(N-100,104,100,94,0)	6	3	3	1

End point values	MenACWY Group			

Subject group type	Reporting group			
Number of subjects analysed	102			
Units: Participants				
Arthralgia at Dose 1(N-98,100,96,86,98)	18			
Fatigue at Dose 1(N-99,102,100,92,100)	50			
Nausea at Dose 1(N-97,101,97,85,99)	14			
Headache at Dose 1(98,102,98,92,99)	36			
Myalgia at Dose 1(N-98,101,97,87,99)	28			
Fever at Dose 1(N-100,103,100,94,101)	3			
Arthralgia at Dose 2(N-98,103,98,92,0)	0			
Fatigue at Dose 2(N-100,104,100,94,0)	0			
Nausea at Dose 2(N-98,102,98,93,0)	0			
Headache at Dose 2(N-98,104,100,93,0)	0			
Myalgia at Dose 2(N-98,103,99,94,0)	0			
Fever at Dose 2(N-100,104,100,94,0)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with unsolicited AEs

End point title	Number of subjects with unsolicited AEs

End point description:

An AE is any untoward medical occurrence in a clinical investigation subject,temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product.An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding),symptom, or disease (new or exacerbated) temporally associated with the use of a medicinal product.For marketed medicinal products, this also includes failure to produce expected benefits (i.e. lack of efficacy), abuse or misuse.An unsolicited AE is an AE that was not solicited using a Subject Diary and that was spontaneously communicated by a subjects/parent(s)/ Legally Acceptable Representative who has signed the informed consent or a solicited local or systemic adverse event that continues beyond the solicited period at day 7 after vaccination.Analysis was performed on unsolicited safety set.No results for dose 2 category for subjects of MenACWY Group as they received only 1 dose at day 1.

End point type	Secondary

End point timeframe:

During the 30 days (including the day of vaccination) after each vaccination i.e after Dose 1 administered at Day 1 (for all groups) and after Dose 2 administered at Day 61 (for all groups except for MenACWY Group)

End point values	MenABCWY Group	rMenBOMV+ACWY_S Group	rMenBOMV+ACWY_D Group	rMenBOMV Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	100	104	100	94
Units: Participants				
Any unsolicited AEs- Dose 1	16	19	16	16
Any unsolicited AEs- Dose 2 (N-100,104,100,94,0)	11	14	13	10

End point values	MenACWY Group			
Subject group type	Reporting group			
Number of subjects analysed	102			
Units: Participants				
Any unsolicited AEs- Dose 1	15			
Any unsolicited AEs- Dose 2 (N-100,104,100,94,0)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with Serious Adverse Events (SAEs), medically attended AEs (MAEs), AEs leading to withdrawal, and Adverse events of special interest (AESIs)

End point title	Number of subjects with Serious Adverse Events (SAEs), medically attended AEs (MAEs), AEs leading to withdrawal, and Adverse events of special interest (AESIs)

End point description:

SAE is defined as any untoward medical occurrence that resulted in death, was life-threatening, required hospitalization or prolongation of existing hospitalization, resulted in disability or incapacity or was a congenital anomaly/birth defect in the offspring of a study subject. Medically attended AEs are defined as symptoms or illnesses requiring hospitalization, or emergency room visit, or visit to/by a health care provider. AESIs are predefined (serious or non-serious) adverse events of scientific and medical concern specific to the product or program, for which ongoing monitoring and rapid communication by the investigator to the sponsor can be appropriate, because such an event might warrant further investigation in order to characterize and understand it. Analysis was performed on the unsolicited safety set.

End point type	Secondary

End point timeframe:

During the whole study period i.e from Day 1 to Day 91

End point values	MenABCWY Group	rMenBOMV+ACWY_S Group	rMenBOMV+ACWY_D Group	rMenBOMV Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	100	104	100	94
Units: Participants				
SAE(s)	0	2	1	2
MAE(s)	14	17	14	13
AE(s) leading to withdrawal	0	0	0	0
AESI(s)	0	0	0	0

End point values	MenACWY Group			

Subject group type	Reporting group			
Number of subjects analysed	102			
Units: Participants				
SAE(s)	0			
MAE(s)	6			
AE(s) leading to withdrawal	0			
AESI(s)	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited Adverse Events were reported during the 7 days post-vaccination period and Unsolicited Adverse Events during the 30 Days post-vaccination period.
Serious Adverse Events: were reported during the whole study period (from Day 1 up to Day 91).

Assessment type	Systematic

Dictionary used

Dictionary name	MedRA 20.1
Dictionary version	20.1

Reporting groups

Reporting group title	MenABCWY Group

Reporting group description:

Healthy subjects between, and including, 10 to 25 years of age at the time of the first vaccination (equally distributed across the 2 age strata of 10 to 17 years and 18 to 25 years) received one dose of MenABCWY twice, 2 months apart (Day 1 and Day 61).

Reporting group title	rMenBOMV+ACWY_S Group

Reporting group description:

Healthy subjects between, and including, 10 to 25 years of age at the time of the first vaccination (equally distributed across the 2 age strata of 10 to 17 years and 18 to 25 years) concomitantly received one dose of rMenB+OMV NZ (Bexsero) and one dose of MenACWY (Menveo) in the same arm twice, 2 months apart (Day 1 and Day 61).

Reporting group title	rMenBOMV+ACWY_D Group

Reporting group description:

Healthy subjects between, and including, 10 to 25 years of age at the time of the first vaccination (equally distributed across the 2 age strata of 10 to 17 years and 18 to 25 years) concomitantly received one dose of rMenB+OMV NZ (Bexsero) and one dose of MenACWY (Menveo) in 2 different arms twice, 2 months apart (Day 1 and Day 61).

Reporting group title	rMenBOMV Group

Reporting group description:

Healthy subjects between, and including, 10 to 25 years of age at the time of the first vaccination (equally distributed across the 2 age strata of 10 to 17 years and 18 to 25 years) received one dose of rMenB+OMV NZ (Bexsero) twice, 2 months apart (Day 1 and Day 61).

Reporting group title	MenACWY Group

Reporting group description:

Healthy subjects between, and including, 10 to 25 years of age at the time of the first vaccination (equally distributed across the 2 age strata of 10 to 17 years and 18 to 25 years) received one dose of MenACWY (Menveo) once (Day 1).

Serious adverse events	MenABCWY Group	rMenBOMV+ACWY_S Group	rMenBOMV+ACWY_D Group
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 100 (0.00%)	2 / 104 (1.92%)	1 / 100 (1.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Concussion			

subjects affected / exposed	0 / 100 (0.00%)	2 / 104 (1.92%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower limb fracture			
subjects affected / exposed	0 / 100 (0.00%)	0 / 104 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tibia fracture			
subjects affected / exposed	0 / 100 (0.00%)	0 / 104 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 100 (0.00%)	0 / 104 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	rMenBOMV Group	MenACWY Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 94 (2.13%)	0 / 102 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Concussion			
subjects affected / exposed	0 / 94 (0.00%)	0 / 102 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower limb fracture			
subjects affected / exposed	1 / 94 (1.06%)	0 / 102 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture			

subjects affected / exposed	0 / 94 (0.00%)	0 / 102 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Syncope			
subjects affected / exposed	1 / 94 (1.06%)	0 / 102 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	MenABCWY Group	rMenBOMV+ACWY_S Group	rMenBOMV+ACWY_D Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	94 / 100 (94.00%)	103 / 104 (99.04%)	98 / 100 (98.00%)
General disorders and administration site conditions			
Face oedema			
subjects affected / exposed	0 / 100 (0.00%)	0 / 104 (0.00%)	0 / 100 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	70 / 100 (70.00%)	74 / 104 (71.15%)	72 / 100 (72.00%)
occurrences (all)	114	122	117
Inflammation			
subjects affected / exposed	1 / 100 (1.00%)	0 / 104 (0.00%)	0 / 100 (0.00%)
occurrences (all)	1	0	0
Injection site pain			
subjects affected / exposed	94 / 100 (94.00%)	102 / 104 (98.08%)	97 / 100 (97.00%)
occurrences (all)	176	197	190
Erythema			
subjects affected / exposed	50 / 100 (50.00%)	71 / 104 (68.27%)	57 / 100 (57.00%)
occurrences (all)	78	108	82
Swelling			
subjects affected / exposed	51 / 100 (51.00%)	63 / 104 (60.58%)	46 / 100 (46.00%)
occurrences (all)	80	98	69
Induration			

subjects affected / exposed	44 / 100 (44.00%)	54 / 104 (51.92%)	49 / 100 (49.00%)
occurrences (all)	65	85	72
Pyrexia			
subjects affected / exposed	12 / 100 (12.00%)	7 / 104 (6.73%)	8 / 100 (8.00%)
occurrences (all)	13	8	8
Injection site induration			
subjects affected / exposed	2 / 100 (2.00%)	5 / 104 (4.81%)	1 / 100 (1.00%)
occurrences (all)	2	5	1
Injection site erythema			
subjects affected / exposed	2 / 100 (2.00%)	3 / 104 (2.88%)	4 / 100 (4.00%)
occurrences (all)	2	3	4
Injection site swelling			
subjects affected / exposed	3 / 100 (3.00%)	2 / 104 (1.92%)	1 / 100 (1.00%)
occurrences (all)	4	2	1
Vaccination site erythema			
subjects affected / exposed	0 / 100 (0.00%)	0 / 104 (0.00%)	3 / 100 (3.00%)
occurrences (all)	0	0	3
Vaccination site swelling			
subjects affected / exposed	0 / 100 (0.00%)	0 / 104 (0.00%)	2 / 100 (2.00%)
occurrences (all)	0	0	2
Vaccination site induration			
subjects affected / exposed	0 / 100 (0.00%)	0 / 104 (0.00%)	1 / 100 (1.00%)
occurrences (all)	0	0	1
Injection site hypersensitivity			
subjects affected / exposed	0 / 100 (0.00%)	0 / 104 (0.00%)	1 / 100 (1.00%)
occurrences (all)	0	0	1
Injection site discolouration			
subjects affected / exposed	1 / 100 (1.00%)	0 / 104 (0.00%)	0 / 100 (0.00%)
occurrences (all)	1	0	0
Immune system disorders			
Food allergy			
subjects affected / exposed	0 / 100 (0.00%)	0 / 104 (0.00%)	0 / 100 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			

Dysmenorrhoea			
subjects affected / exposed	0 / 100 (0.00%)	0 / 104 (0.00%)	1 / 100 (1.00%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	0 / 100 (0.00%)	1 / 104 (0.96%)	1 / 100 (1.00%)
occurrences (all)	0	1	1
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 100 (1.00%)	0 / 104 (0.00%)	0 / 100 (0.00%)
occurrences (all)	1	0	0
Investigations			
Weight decreased			
subjects affected / exposed	0 / 100 (0.00%)	0 / 104 (0.00%)	1 / 100 (1.00%)
occurrences (all)	0	0	1
Weight increased			
subjects affected / exposed	0 / 100 (0.00%)	0 / 104 (0.00%)	1 / 100 (1.00%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Ligament sprain			
subjects affected / exposed	1 / 100 (1.00%)	0 / 104 (0.00%)	0 / 100 (0.00%)
occurrences (all)	1	0	0
Arthropod bite			
subjects affected / exposed	0 / 100 (0.00%)	0 / 104 (0.00%)	0 / 100 (0.00%)
occurrences (all)	0	0	0
Contusion			
subjects affected / exposed	0 / 100 (0.00%)	0 / 104 (0.00%)	0 / 100 (0.00%)
occurrences (all)	0	0	0
Foot fracture			
subjects affected / exposed	0 / 100 (0.00%)	0 / 104 (0.00%)	1 / 100 (1.00%)
occurrences (all)	0	0	1
Head injury			
subjects affected / exposed	0 / 100 (0.00%)	1 / 104 (0.96%)	0 / 100 (0.00%)
occurrences (all)	0	1	0
Limb injury			

subjects affected / exposed	0 / 100 (0.00%)	1 / 104 (0.96%)	0 / 100 (0.00%)
occurrences (all)	0	1	0
Thermal burn			
subjects affected / exposed	0 / 100 (0.00%)	1 / 104 (0.96%)	0 / 100 (0.00%)
occurrences (all)	0	1	0
Arthropod sting			
subjects affected / exposed	1 / 100 (1.00%)	0 / 104 (0.00%)	0 / 100 (0.00%)
occurrences (all)	1	0	0
Vaccination complication			
subjects affected / exposed	2 / 100 (2.00%)	0 / 104 (0.00%)	0 / 100 (0.00%)
occurrences (all)	2	0	0
Nervous system disorders			
Migraine			
subjects affected / exposed	0 / 100 (0.00%)	2 / 104 (1.92%)	0 / 100 (0.00%)
occurrences (all)	0	2	0
Syncope			
subjects affected / exposed	0 / 100 (0.00%)	2 / 104 (1.92%)	0 / 100 (0.00%)
occurrences (all)	0	2	0
Headache			
subjects affected / exposed	60 / 100 (60.00%)	57 / 104 (54.81%)	54 / 100 (54.00%)
occurrences (all)	92	82	75
Dizziness			
subjects affected / exposed	1 / 100 (1.00%)	1 / 104 (0.96%)	0 / 100 (0.00%)
occurrences (all)	1	1	0
Paraesthesia			
subjects affected / exposed	1 / 100 (1.00%)	0 / 104 (0.00%)	0 / 100 (0.00%)
occurrences (all)	1	0	0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 100 (1.00%)	0 / 104 (0.00%)	0 / 100 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Toothache			
subjects affected / exposed	1 / 100 (1.00%)	1 / 104 (0.96%)	0 / 100 (0.00%)
occurrences (all)	1	1	0
Abdominal pain			

subjects affected / exposed	0 / 100 (0.00%)	1 / 104 (0.96%)	0 / 100 (0.00%)
occurrences (all)	0	1	0
Anal fissure			
subjects affected / exposed	0 / 100 (0.00%)	0 / 104 (0.00%)	1 / 100 (1.00%)
occurrences (all)	0	0	1
Dyspepsia			
subjects affected / exposed	0 / 100 (0.00%)	0 / 104 (0.00%)	1 / 100 (1.00%)
occurrences (all)	0	0	1
Enteritis			
subjects affected / exposed	1 / 100 (1.00%)	0 / 104 (0.00%)	0 / 100 (0.00%)
occurrences (all)	1	0	0
Gastritis			
subjects affected / exposed	0 / 100 (0.00%)	1 / 104 (0.96%)	0 / 100 (0.00%)
occurrences (all)	0	1	0
Nausea			
subjects affected / exposed	24 / 100 (24.00%)	26 / 104 (25.00%)	26 / 100 (26.00%)
occurrences (all)	32	36	29
Diarrhoea			
subjects affected / exposed	0 / 100 (0.00%)	1 / 104 (0.96%)	0 / 100 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	1 / 100 (1.00%)	1 / 104 (0.96%)	0 / 100 (0.00%)
occurrences (all)	1	1	0
Eczema			
subjects affected / exposed	0 / 100 (0.00%)	1 / 104 (0.96%)	0 / 100 (0.00%)
occurrences (all)	0	1	0
Erythema			
subjects affected / exposed	0 / 100 (0.00%)	0 / 104 (0.00%)	0 / 100 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 100 (0.00%)	1 / 104 (0.96%)	1 / 100 (1.00%)
occurrences (all)	0	1	1
Arthralgia			

subjects affected / exposed	29 / 100 (29.00%)	29 / 104 (27.88%)	18 / 100 (18.00%)
occurrences (all)	42	34	21
Musculoskeletal pain			
subjects affected / exposed	0 / 100 (0.00%)	0 / 104 (0.00%)	0 / 100 (0.00%)
occurrences (all)	0	0	0
Tendonitis			
subjects affected / exposed	1 / 100 (1.00%)	0 / 104 (0.00%)	0 / 100 (0.00%)
occurrences (all)	1	0	0
Pain in extremity			
subjects affected / exposed	0 / 100 (0.00%)	0 / 104 (0.00%)	1 / 100 (1.00%)
occurrences (all)	0	0	1
Myalgia			
subjects affected / exposed	50 / 100 (50.00%)	49 / 104 (47.12%)	45 / 100 (45.00%)
occurrences (all)	75	67	64
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	5 / 100 (5.00%)	3 / 104 (2.88%)	0 / 100 (0.00%)
occurrences (all)	5	3	0
Viral infection			
subjects affected / exposed	2 / 100 (2.00%)	1 / 104 (0.96%)	0 / 100 (0.00%)
occurrences (all)	2	1	0
Gastroenteritis			
subjects affected / exposed	1 / 100 (1.00%)	0 / 104 (0.00%)	1 / 100 (1.00%)
occurrences (all)	1	0	1
Tonsillitis			
subjects affected / exposed	2 / 100 (2.00%)	0 / 104 (0.00%)	0 / 100 (0.00%)
occurrences (all)	2	0	0
Bronchitis			
subjects affected / exposed	0 / 100 (0.00%)	0 / 104 (0.00%)	1 / 100 (1.00%)
occurrences (all)	0	0	1
Rhinitis			
subjects affected / exposed	0 / 100 (0.00%)	0 / 104 (0.00%)	1 / 100 (1.00%)
occurrences (all)	0	0	1
Lyme disease			
subjects affected / exposed	0 / 100 (0.00%)	1 / 104 (0.96%)	0 / 100 (0.00%)
occurrences (all)	0	1	0

Otitis externa			
subjects affected / exposed	0 / 100 (0.00%)	0 / 104 (0.00%)	1 / 100 (1.00%)
occurrences (all)	0	0	1
Skin infection			
subjects affected / exposed	0 / 100 (0.00%)	0 / 104 (0.00%)	1 / 100 (1.00%)
occurrences (all)	0	0	1
Pericoronitis			
subjects affected / exposed	0 / 100 (0.00%)	0 / 104 (0.00%)	0 / 100 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 100 (0.00%)	0 / 104 (0.00%)	1 / 100 (1.00%)
occurrences (all)	0	0	1
Pharyngitis streptococcal			
subjects affected / exposed	0 / 100 (0.00%)	1 / 104 (0.96%)	0 / 100 (0.00%)
occurrences (all)	0	1	0
Viral pharyngitis			
subjects affected / exposed	1 / 100 (1.00%)	0 / 104 (0.00%)	0 / 100 (0.00%)
occurrences (all)	1	0	0
Paronychia			
subjects affected / exposed	0 / 100 (0.00%)	0 / 104 (0.00%)	1 / 100 (1.00%)
occurrences (all)	0	0	1
Respiratory tract infection viral			
subjects affected / exposed	0 / 100 (0.00%)	1 / 104 (0.96%)	0 / 100 (0.00%)
occurrences (all)	0	1	0
Sinusitis			
subjects affected / exposed	1 / 100 (1.00%)	0 / 104 (0.00%)	0 / 100 (0.00%)
occurrences (all)	1	0	0
Oral herpes			
subjects affected / exposed	0 / 100 (0.00%)	1 / 104 (0.96%)	0 / 100 (0.00%)
occurrences (all)	0	1	0
Acute sinusitis			
subjects affected / exposed	0 / 100 (0.00%)	0 / 104 (0.00%)	0 / 100 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 100 (0.00%)	3 / 104 (2.88%)	1 / 100 (1.00%)
occurrences (all)	0	3	1

Non-serious adverse events	rMenBOMV Group	MenACWY Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	94 / 94 (100.00%)	80 / 102 (78.43%)	
General disorders and administration site conditions			
Face oedema			
subjects affected / exposed	1 / 94 (1.06%)	0 / 102 (0.00%)	
occurrences (all)	1	0	
Fatigue			
subjects affected / exposed	63 / 94 (67.02%)	50 / 102 (49.02%)	
occurrences (all)	102	50	
Inflammation			
subjects affected / exposed	0 / 94 (0.00%)	0 / 102 (0.00%)	
occurrences (all)	0	0	
Injection site pain			
subjects affected / exposed	93 / 94 (98.94%)	53 / 102 (51.96%)	
occurrences (all)	175	53	
Erythema			
subjects affected / exposed	58 / 94 (61.70%)	28 / 102 (27.45%)	
occurrences (all)	81	28	
Swelling			
subjects affected / exposed	46 / 94 (48.94%)	23 / 102 (22.55%)	
occurrences (all)	65	23	
Induration			
subjects affected / exposed	38 / 94 (40.43%)	19 / 102 (18.63%)	
occurrences (all)	56	19	
Pyrexia			
subjects affected / exposed	2 / 94 (2.13%)	3 / 102 (2.94%)	
occurrences (all)	2	3	
Injection site induration			
subjects affected / exposed	4 / 94 (4.26%)	0 / 102 (0.00%)	
occurrences (all)	4	0	
Injection site erythema			
subjects affected / exposed	1 / 94 (1.06%)	0 / 102 (0.00%)	
occurrences (all)	1	0	
Injection site swelling			

subjects affected / exposed	1 / 94 (1.06%)	0 / 102 (0.00%)	
occurrences (all)	1	0	
Vaccination site erythema			
subjects affected / exposed	0 / 94 (0.00%)	1 / 102 (0.98%)	
occurrences (all)	0	1	
Vaccination site swelling			
subjects affected / exposed	0 / 94 (0.00%)	2 / 102 (1.96%)	
occurrences (all)	0	2	
Vaccination site induration			
subjects affected / exposed	0 / 94 (0.00%)	1 / 102 (0.98%)	
occurrences (all)	0	1	
Injection site hypersensitivity			
subjects affected / exposed	0 / 94 (0.00%)	0 / 102 (0.00%)	
occurrences (all)	0	0	
Injection site discolouration			
subjects affected / exposed	0 / 94 (0.00%)	0 / 102 (0.00%)	
occurrences (all)	0	0	
Immune system disorders			
Food allergy			
subjects affected / exposed	0 / 94 (0.00%)	1 / 102 (0.98%)	
occurrences (all)	0	1	
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	0 / 94 (0.00%)	0 / 102 (0.00%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	1 / 94 (1.06%)	0 / 102 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 94 (0.00%)	0 / 102 (0.00%)	
occurrences (all)	0	0	
Investigations			
Weight decreased			

subjects affected / exposed	0 / 94 (0.00%)	0 / 102 (0.00%)	
occurrences (all)	0	0	
Weight increased			
subjects affected / exposed	0 / 94 (0.00%)	0 / 102 (0.00%)	
occurrences (all)	0	0	
Injury, poisoning and procedural complications			
Ligament sprain			
subjects affected / exposed	2 / 94 (2.13%)	0 / 102 (0.00%)	
occurrences (all)	2	0	
Arthropod bite			
subjects affected / exposed	1 / 94 (1.06%)	0 / 102 (0.00%)	
occurrences (all)	1	0	
Contusion			
subjects affected / exposed	1 / 94 (1.06%)	0 / 102 (0.00%)	
occurrences (all)	1	0	
Foot fracture			
subjects affected / exposed	0 / 94 (0.00%)	0 / 102 (0.00%)	
occurrences (all)	0	0	
Head injury			
subjects affected / exposed	0 / 94 (0.00%)	0 / 102 (0.00%)	
occurrences (all)	0	0	
Limb injury			
subjects affected / exposed	0 / 94 (0.00%)	0 / 102 (0.00%)	
occurrences (all)	0	0	
Thermal burn			
subjects affected / exposed	0 / 94 (0.00%)	0 / 102 (0.00%)	
occurrences (all)	0	0	
Arthropod sting			
subjects affected / exposed	0 / 94 (0.00%)	0 / 102 (0.00%)	
occurrences (all)	0	0	
Vaccination complication			
subjects affected / exposed	0 / 94 (0.00%)	0 / 102 (0.00%)	
occurrences (all)	0	0	
Nervous system disorders			

Migraine			
subjects affected / exposed	0 / 94 (0.00%)	0 / 102 (0.00%)	
occurrences (all)	0	0	
Syncope			
subjects affected / exposed	2 / 94 (2.13%)	1 / 102 (0.98%)	
occurrences (all)	2	1	
Headache			
subjects affected / exposed	52 / 94 (55.32%)	36 / 102 (35.29%)	
occurrences (all)	75	36	
Dizziness			
subjects affected / exposed	0 / 94 (0.00%)	0 / 102 (0.00%)	
occurrences (all)	0	0	
Paraesthesia			
subjects affected / exposed	0 / 94 (0.00%)	0 / 102 (0.00%)	
occurrences (all)	0	0	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 94 (0.00%)	0 / 102 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal disorders			
Toothache			
subjects affected / exposed	2 / 94 (2.13%)	1 / 102 (0.98%)	
occurrences (all)	2	1	
Abdominal pain			
subjects affected / exposed	0 / 94 (0.00%)	0 / 102 (0.00%)	
occurrences (all)	0	0	
Anal fissure			
subjects affected / exposed	0 / 94 (0.00%)	0 / 102 (0.00%)	
occurrences (all)	0	0	
Dyspepsia			
subjects affected / exposed	0 / 94 (0.00%)	0 / 102 (0.00%)	
occurrences (all)	0	0	
Enteritis			
subjects affected / exposed	0 / 94 (0.00%)	0 / 102 (0.00%)	
occurrences (all)	0	0	
Gastritis			

subjects affected / exposed	0 / 94 (0.00%)	0 / 102 (0.00%)	
occurrences (all)	0	0	
Nausea			
subjects affected / exposed	26 / 94 (27.66%)	14 / 102 (13.73%)	
occurrences (all)	30	14	
Diarrhoea			
subjects affected / exposed	0 / 94 (0.00%)	2 / 102 (1.96%)	
occurrences (all)	0	2	
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	0 / 94 (0.00%)	0 / 102 (0.00%)	
occurrences (all)	0	0	
Eczema			
subjects affected / exposed	0 / 94 (0.00%)	0 / 102 (0.00%)	
occurrences (all)	0	0	
Erythema			
subjects affected / exposed	1 / 94 (1.06%)	0 / 102 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 94 (1.06%)	0 / 102 (0.00%)	
occurrences (all)	1	0	
Arthralgia			
subjects affected / exposed	19 / 94 (20.21%)	18 / 102 (17.65%)	
occurrences (all)	26	18	
Musculoskeletal pain			
subjects affected / exposed	0 / 94 (0.00%)	1 / 102 (0.98%)	
occurrences (all)	0	1	
Tendonitis			
subjects affected / exposed	0 / 94 (0.00%)	0 / 102 (0.00%)	
occurrences (all)	0	0	
Pain in extremity			
subjects affected / exposed	3 / 94 (3.19%)	0 / 102 (0.00%)	
occurrences (all)	4	0	
Myalgia			

subjects affected / exposed	41 / 94 (43.62%)	28 / 102 (27.45%)	
occurrences (all)	59	28	
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	3 / 94 (3.19%)	3 / 102 (2.94%)	
occurrences (all)	3	3	
Viral infection			
subjects affected / exposed	0 / 94 (0.00%)	1 / 102 (0.98%)	
occurrences (all)	0	1	
Gastroenteritis			
subjects affected / exposed	1 / 94 (1.06%)	0 / 102 (0.00%)	
occurrences (all)	1	0	
Tonsillitis			
subjects affected / exposed	0 / 94 (0.00%)	1 / 102 (0.98%)	
occurrences (all)	0	1	
Bronchitis			
subjects affected / exposed	0 / 94 (0.00%)	1 / 102 (0.98%)	
occurrences (all)	0	1	
Rhinitis			
subjects affected / exposed	0 / 94 (0.00%)	2 / 102 (1.96%)	
occurrences (all)	0	2	
Lyme disease			
subjects affected / exposed	0 / 94 (0.00%)	0 / 102 (0.00%)	
occurrences (all)	0	0	
Otitis externa			
subjects affected / exposed	0 / 94 (0.00%)	0 / 102 (0.00%)	
occurrences (all)	0	0	
Skin infection			
subjects affected / exposed	0 / 94 (0.00%)	0 / 102 (0.00%)	
occurrences (all)	0	0	
Pericoronitis			
subjects affected / exposed	1 / 94 (1.06%)	0 / 102 (0.00%)	
occurrences (all)	1	0	
Pharyngitis			
subjects affected / exposed	0 / 94 (0.00%)	0 / 102 (0.00%)	
occurrences (all)	0	0	

Pharyngitis streptococcal			
subjects affected / exposed	0 / 94 (0.00%)	0 / 102 (0.00%)	
occurrences (all)	0	0	
Viral pharyngitis			
subjects affected / exposed	0 / 94 (0.00%)	0 / 102 (0.00%)	
occurrences (all)	0	0	
Paronychia			
subjects affected / exposed	0 / 94 (0.00%)	0 / 102 (0.00%)	
occurrences (all)	0	0	
Respiratory tract infection viral			
subjects affected / exposed	0 / 94 (0.00%)	0 / 102 (0.00%)	
occurrences (all)	0	0	
Sinusitis			
subjects affected / exposed	0 / 94 (0.00%)	0 / 102 (0.00%)	
occurrences (all)	0	0	
Oral herpes			
subjects affected / exposed	0 / 94 (0.00%)	0 / 102 (0.00%)	
occurrences (all)	0	0	
Acute sinusitis			
subjects affected / exposed	1 / 94 (1.06%)	0 / 102 (0.00%)	
occurrences (all)	1	0	
Nasopharyngitis			
subjects affected / exposed	1 / 94 (1.06%)	0 / 102 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 May 2018	• The protocol has been updated based on feedback received from the State Institute for Drug Control (SUKL) regarding contraception requirements, exclusion of other vaccines before and after study vaccine(s) administration, exclusion of subjects with medical bleeding conditions, and to indicate that paracetamol is the preferred antipyret-ic/analgesic. • The distribution and return of Subject Diaries has been clarified. • The protocol was updated to include the use of a pregnancy notification form and to clarify that paper pregnancy reports will be used. • Clarifications have been made to the analysis pop-ulation definitions and the modeling analysis plans. • Other minor changes have been made to correct typos and improve clarity and alignment within the document.
29 August 2018	• A tertiary objective was added to allow potential exploratory evaluation of immune responses in-duced by the study vaccine(s) against a panel of strains of Neisseria species in a subset of subjects. • Protocol Clarification Letter 1 was incorporated, which removed reference to a pregnancy electronic case report form. • The window for Subject Diary reminder calls was clarified. • Other minor changes were made to correct typos and improve clarity and alignment within the document.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported