Clinical trial results:
A Phase 2, Open-label, Controlled, Multi-Center Extension Study to Evaluate 4-Year Antibody Persistence and Booster Response Following MenABCWY Vaccination in Healthy Adolescents and Young Adults who Previously Participated in Studies V102_02 (NCT01210885) and V102_02E1 (NCT01367158).

Summary

EudraCT number	2016-004420-29
Trial protocol	Outside EU/EEA
Global end of trial date	10 December 2015

Results information

Result version number	v3 (current)
This version publication date	13 January 2018
First version publication date	16 March 2017
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	205213

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02451514
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline Biologicals
Sponsor organisation address	Rue de l'Institut 89, Rixensart, Belgium, B-1330
Public contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 44 2089904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 44 2089904466, GSKClinicalSupportHD@gsk.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	07 November 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 November 2015
Global end of trial reached?	Yes
Global end of trial date	10 December 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

• To assess the antibody persistence against N. meningitidis serogroups A, C, W and Y and serogroup B test strains in subjects who previously received MenABCWY+OMV or MenACWY approximately 4 years earlier, as measured by the percentage of subjects with hSBA titers ≥ lower limit quantitation (LLQ) and other thresholds, hSBA Geometric Mean Titers (GMTs) and geometric mean ratios (GMRs).
• To evaluate the immune response against N. meningitidis serogroups A, C, W and Y and serogroup B test strains 30 days after a single dose of MenABCWY+OMV in previously vaccinated subjects, and in vaccine-naïve subjects (VNS) of similar age, as measured by the percentage of subjects with hSBA titers ≥LLQ and other thresholds, hSBA GMTs and GMRs.

Protection of trial subjects:

The study was conducted in compliance with the protocol, Good Clinical Practices (GCPs) and applicable regulatory requirement(s). This clinical study was designed, implemented and reported in accordance with the ICH Harmonized Tripartite Guidelines for Good Clinical Practice, with applicable local regulations, Novartis codes on protection of human rights, and with the ethical principles laid down in the Declaration of Helsinki (European Council 2001, US Code of Federal Regulations, ICH 1997).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 June 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Chile: 13
Country: Number of subjects enrolled	Panama: 88
Country: Number of subjects enrolled	Colombia: 28
Worldwide total number of subjects	129
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	45
Adults (18-64 years)	84
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were recruited from 5 sites in Panama, 3 sites in Colombia and 1 site in Chile.

Pre-assignment

Screening details:

Healthy adolescents & young adults, who received 2 doses of MenABCWY+OMV vaccine or 1 dose of MENACWY in parent study V102_02(NCT01210885) & only Tdap vaccination in V102_02E1(NCT01367158) study were included in the present study, along with Naive subjects of

Period 1

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

Blinding implementation details:

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

Arms

Are arms mutually exclusive?	Yes
Arm title	MenABCWY+OMV Group

Arm description:

Subjects who received 2 doses of MenABCWY+OMV vaccine in the parent study V102_02 (NCT01210885) and received no subsequent meningococcal vaccines, received a booster dose of MenABCWY+OMV vaccine in the current study at Day 1.

Arm type	Experimental
Investigational medicinal product name	Meningococcal (groups A, C , W , Y-135) Oligosaccharide Diphtheria CRM197 Conjugate combined with Meningococcal (group B) Multi-Component Recombinant 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:

2 doses (0.5 ml each), 1 month apart

Arm title	MenACWY Group

Arm description:

Subjects who received MenACWY vaccine in the parent study V102_02 (NCT01210885) and received no subsequent meningococcal vaccines, received 2 doses of MenABCWY+OMV vaccine, one month apart (Day 1 and Day 31), in the current study.

Arm type	Experimental
Investigational medicinal product name	Meningococcal (groups A, C , W , Y-135) Oligosaccharide Diphtheria CRM197 Conjugate combined with Meningococcal (group B) Multi-Component Recombinant 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:

2 doses (0.5 ml each), 1 month apart

Arm title	Naive Group

Arm description:

Subjects similar in age to subjects in the MenABCWY+OMV and MenACWY groups, who had not previously received any meningococcal vaccine and who received 2 doses of MenABCWY+OMV vaccine, 1 month apart (Day 1 and Day 31), in the current study.

Arm type	Experimental
Investigational medicinal product name	Meningococcal (groups A, C , W , Y-135) Oligosaccharide Diphtheria CRM197 Conjugate combined with Meningococcal (group B) Multi-Component Recombinant 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:

2 doses (0.5 ml each), 1 month apart

Number of subjects in period 1	MenABCWY+OMV Group	MenACWY Group	Naive Group
Started	33	46	50
Completed	33	46	50

Baseline characteristics

Reporting groups	
Reporting group title	MenABCWY+OMV Group
Reporting group description:	
Subjects who received 2 doses of MenABCWY+OMV vaccine in the parent study V102_02 (NCT01210885) and received no subsequent meningococcal vaccines, received a booster dose of MenABCWY+OMV vaccine in the current study at Day 1.	
Reporting group title	MenACWY Group
Reporting group description:	
Subjects who received MenACWY vaccine in the parent study V102_02 (NCT01210885) and received no subsequent meningococcal vaccines, received 2 doses of MenABCWY+OMV vaccine, one month apart (Day 1 and Day 31), in the current study.	
Reporting group title	Naive Group
Reporting group description:	
Subjects similar in age to subjects in the MenABCWY+OMV and MenACWY groups, who had not previously received any meningococcal vaccine and who received 2 doses of MenABCWY+OMV vaccine, 1 month apart (Day 1 and Day 31), in the current study.	

Reporting group values	MenABCWY+OMV Group	MenACWY Group	Naive Group
Number of subjects	33	46	50
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	12	14	19
Adults (18-64 years)	21	32	31
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	18.61	18.72	17.96
standard deviation	± 2.207	± 1.87	± 2.04
Gender categorical Units: Subjects			
Female	22	27	25
Male	11	19	25
Race/Ethnicity, Customized Units: Subjects			
Race American Indian or Alaska Native	2	4	3
Race Black or African American	4	2	4
Race White	7	6	6
Race Other	20	34	37

Reporting group values	Total		
Number of subjects	129		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	45		
Adults (18-64 years)	84		
From 65-84 years	0		
85 years and over	0		
Age continuous Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical Units: Subjects			
Female	74		
Male	55		
Race/Ethnicity, Customized Units: Subjects			
Race American Indian or Alaska Native	9		
Race Black or African American	10		
Race White	19		
Race Other	91		

Subject analysis sets

Subject analysis set title	MenABCWY+OMV Group (A)
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects who received 2 doses of MenABCWY+OMV vaccine in the parent study V102_02 (NCT01210885) and received no subsequent meningococcal vaccines, received a booster dose of MenABCWY+OMV vaccine in the current study at Day 1. Blood samples will be collected from subjects at Day 1 (before vaccination), Day 4, Day 8 and Day 31.

Subject analysis set title	MenACWY Group (B1)
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects who received MenACWY vaccine in the parent study V102_02 (NCT01210885) and received no subsequent meningococcal vaccines, received 2 doses of MenABCWY+OMV vaccine, one month apart, in the current study. Blood samples will be collected from subjects at Day 1 (before vaccination), Day 4, Day 31 (before vaccination) and Day 61.

Subject analysis set title	MenACWY group (B2)
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects who received MenACWY vaccine in the parent study V102_02 (NCT01210885) and received no subsequent meningococcal vaccines, received 2 doses of MenABCWY+OMV vaccine, one month apart, in the current study. Blood samples will be collected from subjects at Day 1 (before vaccination), Day 8, Day 31 (before vaccination) and Day 61.

Subject analysis set title	Naive Group (C1)
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects similar in age to subjects in the MenABCWY+OMV and MenACWY groups, who had not previously received any meningococcal vaccine and who received 2 doses of MenABCWY+OMV vaccine, 1 month apart (Day 1 and Day 31), in the current study. Blood samples will be collected from subjects at Day 1 (before vaccination), Day 31 (before vaccination), Day 34 and Day 61.

Subject analysis set title	Naive Group (C2)
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects similar in age to subjects in the MenABCWY+OMV and MenACWY groups, who had not previously received any meningococcal vaccine and who received 2 doses of MenABCWY+OMV vaccine, 1 month apart (Day 1 and Day 31), in the current study. Blood samples will be collected from subjects at Day 1 (before vaccination), Day 31 (before vaccination), Day 38 and Day 61.

Reporting group values	MenABCWY+OMV Group (A)	MenACWY Group (B1)	MenACWY group (B2)
Number of subjects	33	23	23
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous Units: years			
arithmetic mean	18.6	18.7	18.7
standard deviation	± 2.21	± 1.72	± 2.05
Gender categorical Units: Subjects			
Female	22	15	12
Male	11	8	11
Race/Ethnicity, Customized Units: Subjects			
Race American Indian or Alaska Native	2	2	2
Race Black or African American	4	1	1
Race White	7	3	3
Race Other	20	17	17

Reporting group values	Naive Group (C1)	Naive Group (C2)	
Number of subjects	26	24	
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			

Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years			
arithmetic mean	17.8	18.1	
standard deviation	± 2.15	± 1.94	
Gender categorical Units: Subjects			
Female	15	10	
Male	11	14	
Race/Ethnicity, Customized Units: Subjects			
Race American Indian or Alaska Native	1	2	
Race Black or African American	2	2	
Race White	3	3	
Race Other	20	17	

End points

End points reporting groups

Reporting group title	MenABCWY+OMV Group

Reporting group description:

Subjects who received 2 doses of MenABCWY+OMV vaccine in the parent study V102_02 (NCT01210885) and received no subsequent meningococcal vaccines, received a booster dose of MenABCWY+OMV vaccine in the current study at Day 1.

Reporting group title	MenACWY Group

Reporting group description:

Subjects who received MenACWY vaccine in the parent study V102_02 (NCT01210885) and received no subsequent meningococcal vaccines, received 2 doses of MenABCWY+OMV vaccine, one month apart (Day 1 and Day 31), in the current study.

Reporting group title	Naive Group

Reporting group description:

Subjects similar in age to subjects in the MenABCWY+OMV and MenACWY groups, who had not previously received any meningococcal vaccine and who received 2 doses of MenABCWY+OMV vaccine, 1 month apart (Day 1 and Day 31), in the current study.

Subject analysis set title	MenABCWY+OMV Group (A)
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects who received 2 doses of MenABCWY+OMV vaccine in the parent study V102_02 (NCT01210885) and received no subsequent meningococcal vaccines, received a booster dose of MenABCWY+OMV vaccine in the current study at Day 1. Blood samples will be collected from subjects at Day 1 (before vaccination), Day 4, Day 8 and Day 31.

Subject analysis set title	MenACWY Group (B1)
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects who received MenACWY vaccine in the parent study V102_02 (NCT01210885) and received no subsequent meningococcal vaccines, received 2 doses of MenABCWY+OMV vaccine, one month apart, in the current study. Blood samples will be collected from subjects at Day 1 (before vaccination), Day 4, Day 31 (before vaccination) and Day 61.

Subject analysis set title	MenACWY group (B2)
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects who received MenACWY vaccine in the parent study V102_02 (NCT01210885) and received no subsequent meningococcal vaccines, received 2 doses of MenABCWY+OMV vaccine, one month apart, in the current study. Blood samples will be collected from subjects at Day 1 (before vaccination), Day 8, Day 31 (before vaccination) and Day 61.

Subject analysis set title	Naive Group (C1)
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects similar in age to subjects in the MenABCWY+OMV and MenACWY groups, who had not previously received any meningococcal vaccine and who received 2 doses of MenABCWY+OMV vaccine, 1 month apart (Day 1 and Day 31), in the current study. Blood samples will be collected from subjects at Day 1 (before vaccination), Day 31 (before vaccination), Day 34 and Day 61.

Subject analysis set title	Naive Group (C2)
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects similar in age to subjects in the MenABCWY+OMV and MenACWY groups, who had not previously received any meningococcal vaccine and who received 2 doses of MenABCWY+OMV vaccine, 1 month apart (Day 1 and Day 31), in the current study. Blood samples will be collected from subjects at Day 1 (before vaccination), Day 31 (before vaccination), Day 38 and Day 61.

Primary: Percentages of Subjects with hSBA ≥ LLQ against N. meningitidis serogroups A, C, W and Y and serogroup B test strains.

End point title	Percentages of Subjects with hSBA ≥ LLQ against N. meningitidis serogroups A, C, W and Y and serogroup B test strains.[1]

End point description:

The HT-hSBA assay format was changed in 2015 in response to CBER comments & validation of this new format & determination of the LLOQ values for the same, are ongoing. However, the old assay format was used for sample testing in this extension trial, to maintain data comparability with the parent trials. The LLOQ cut-off values for the old assay format correspond to 8 for ACWY serogroups & 5 for B strains, & this data is already available & included in the submission. The ongoing validation procedure & determination of new LLOQ values are pertinent to the new assay format for HT-hSBA & are not considered relevant to the data obtained from the testing of the V102_02E2 study. Therefore, in the Company's judgment, the results generated with pre-defined LLOQs of 8 (for ACWY) & 5 (for B strains) are final & there will be no additional data generation with new HT-hSBA LLOQ cut-offs.

End point type	Primary

End point timeframe:

At Day 1 (4 years persistence)

Notes:

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

End point values	MenABCWY+OMV Group	MenACWY Group	Naive Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[2]	0[3]	0[4]	
Units: Percentages of subjects				
number (confidence interval 95%)	(to)	(to)	(to)	

Notes:

[2] - No additional data generation with new HT-hSBA LLOQ cut-offs

[3] - No additional data generation with new HT-hSBA LLOQ cut-offs

[4] - No additional data generation with new HT-hSBA LLOQ cut-offs

Statistical analyses

No statistical analyses for this end point

Primary: Percentages of Subjects with hSBA ≥ 8 against N. meningitidis serogroups A, C, W and Y.

End point title	Percentages of Subjects with hSBA ≥ 8 against N. meningitidis serogroups A, C, W and Y.[5]

End point description:

Antibody levels against N. meningitidis serogroups A, C, W and Y in subjects who previously received MenABCWY+OMV or MenACWY approximately 4 years earlier, and in Naïve subjects as measured by the percentages of subjects with hSBA ≥ 8.
The analysis was performed on Full Analysis Set (FAS) immunogenicity persistence population, which included all subjects in the Enrolled population who provided at least one evaluable serum sample at baseline (Visit 1 in this study) and whose assay results were available for at least one strain.

End point type	Primary

End point timeframe:

At Day 1 (4 years persistence)

Notes:

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

End point values	MenABCWY+OMV Group	MenACWY Group	Naive Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	46	50	
Units: Percentages of subjects				
number (confidence interval 95%)				
Serogroup A (N=33;46;50)	27 (13.3 to 45.5)	41 (27.0 to 56.8)	2 (0.05 to 10.6)	
Serogroup C (N=32;46;49)	69 (50.0 to 83.9)	43 (28.9 to 58.9)	45 (30.7 to 59.8)	
Serogroup W (N=32;46;47)	75 (56.6 to 88.5)	78 (63.6 to 89.1)	53 (38.1 to 67.9)	
Serogroup Y (N=32;44;47)	38 (21.1 to 56.3)	59 (43.2 to 73.7)	19 (9.1 to 33.3)	

Statistical analyses

No statistical analyses for this end point

Primary: Percentages of Subjects with hSBA ≥ 5 against N. meningitidis serogroup B test strains.

End point title	Percentages of Subjects with hSBA ≥ 5 against N. meningitidis serogroup B test strains.[6]

End point description:

Antibody levels against N. meningitidis serogroup B test strains in subjects who previously received MenABCWY+OMV or MenACWY approximately 4 years earlier, and in Naïve subjects as measured by the percentages of Subjects with hSBA ≥ 5. The Meningococcal B Strains were M14459, M01-0240364, NZ98/254, M10713, H44/76 and 5/99.
The analysis was performed on FAS immunogenicity persistence population, which included all subjects in the Enrolled population who provided at least one evaluable serum sample at baseline (Visit 1 in this study) and whose assay results were available for at least one strain.

End point type	Primary

End point timeframe:

At Day 1 (4 years persistence)

Notes:

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

End point values	MenABCWY+OMV Group	MenACWY Group	Naive Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	46	50	
Units: Percentages of subjects				
number (confidence interval 95%)				
Serogroup B, M14459 (N=33;46;50)	18 (7.0 to 35.5)	4 (0.5 to 14.8)	8 (2.2 to 19.2)	
Serogroup B, M01-0240364 (N=31;44;50)	13 (3.6 to 29.8)	5 (0.6 to 15.5)	4 (0.49 to 13.7)	

Serogroup B, NZ98/254 (N=33;46;50)	15 (5.1 to 31.9)	2 (0.06 to 11.5)	6 (1.3 to 16.5)	
Serogroup B, M10713 (N=33;46;50)	48 (30.8 to 66.5)	33 (19.5 to 48.0)	38 (24.7 to 52.8)	
Serogroup B, H44/76 (N=33;46;50)	27 (13.3 to 45.5)	4 (0.5 to 14.8)	10 (3.3 to 21.8)	
Serogroup B, 5/99 (N=33;46;50)	70 (51.3 to 84.4)	17 (7.8 to 31.4)	16 (7.2 to 29.1)	

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean hSBA Titers (GMTs) against N. meningitidis serogroups A, C, W and Y and serogroup B test strains.

End point title	Geometric Mean hSBA Titers (GMTs) against N. meningitidis serogroups A, C, W and Y and serogroup B test strains.

End point description:

GMTs against N. meningitidis serogroups A, C, W and Y and serogroup B test strains in subjects who previously received MenABCWY+OMV or MenACWY approximately 4 years earlier, and in Naïve subjects. The Meningococcal B Strains were M14459, M01-0240364, NZ98/254, M10713, H44/76 and 5/99. The analysis was performed on FAS immunogenicity persistence population, which included all subjects in the Enrolled population who provided at least one evaluable serum sample at baseline (Visit 1 in this study) and whose assay results were available for at least one strain.

End point type	Primary

End point timeframe:

At Day 1

End point values	MenABCWY+OMV Group	MenACWY Group	Naive Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	46	50	
Units: Titers				
geometric mean (confidence interval 95%)				
Serogroup B, M14459 (N=33;46;50)	2.04 (1.46 to 2.83)	1.37 (1.12 to 1.69)	1.48 (1.18 to 1.85)	
Serogroup B, M01-0240364 (N=31;44;50)	2.26 (1.26 to 4.08)	1.14 (0.97 to 1.35)	1.23 (1.02 to 1.47)	
Serogroup B, NZ98/254 (N=33;46;50)	1.81 (1.30 to 2.51)	1.35 (1.15 to 1.59)	1.45 (1.18 to 1.77)	
Serogroup B, M10713 (N=33;46;50)	3.66 (2.38 to 5.62)	2.56 (1.74 to 3.75)	3.10 (2.16 to 4.45)	
Serogroup B, H44/76 (N=33;46;50)	2.33 (1.57 to 3.45)	1.21 (1.03 to 1.42)	1.44 (1.14 to 1.80)	
Serogroup B, 5/99 (N=33;46;50)	13 (7.29 to 22)	1.78 (1.36 to 2.34)	1.90 (1.42 to 2.53)	
Serogroup A (N=33;46;50)	4.06 (2.22 to 7.44)	6.64 (3.56 to 12)	1.20 (1.05 to 1.37)	
Serogroup C (N=32;46;49)	17 (7.80 to 37)	6.62 (4.10 to 11)	5.11 (3.49 to 7.48)	
Serogroup W (N=32;46;47)	28 (15 to 53)	25 (15 to 40)	8.37 (4.78 to 15)	

Serogroup Y (N=32;44;47)	6.17 (3.00 to 13)	12 (6.29 to 22)	2.00 (1.40 to 2.85)	

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description: Between-group Geometric Mean Ratios (GMRs) Against N. Meningitidis Serogroup B, M14459.	
Comparison groups	MenABCWY+OMV Group v MenACWY Group
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	1.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.03
upper limit	2.12

Statistical analysis title	Statistical analysis 2
Statistical analysis description: Between-group Geometric Mean Ratios (GMRs) Against N. Meningitidis Serogroup B, M14459.	
Comparison groups	Naive Group v MenACWY Group
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	0.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.67
upper limit	1.28

Statistical analysis title	Statistical analysis 3
Statistical analysis description: Between-group Geometric Mean Ratios (GMRs) Against N. Meningitidis Serogroup B, M14459.	
Comparison groups	MenABCWY+OMV Group v Naive Group

Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	1.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.97
upper limit	1.96

Statistical analysis title	Statistical analysis 4
Statistical analysis description:	
Between-group Geometric Mean Ratios (GMRs) Against N. Meningitidis Serogroup B, M01-0240364.	
Comparison groups	MenABCWY+OMV Group v MenACWY Group
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	1.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.27
upper limit	3.09

Statistical analysis title	Statistical analysis 5
Statistical analysis description:	
Between-group Geometric Mean Ratios (GMRs) Against N. Meningitidis Serogroup B, M01-0240364.	
Comparison groups	Naive Group v MenACWY Group
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	0.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.63
upper limit	1.37

Statistical analysis title	Statistical analysis 6
Statistical analysis description: Between-group Geometric Mean Ratios (GMRs) Against N. Meningitidis Serogroup B, M01-0240364.	
Comparison groups	MenABCWY+OMV Group v Naive Group
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	1.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.2
upper limit	2.84

Statistical analysis title	Statistical analysis 7
Statistical analysis description: Between-group Geometric Mean Ratios (GMRs) Against N. Meningitidis Serogroup B, NZ98/254.	
Comparison groups	MenABCWY+OMV Group v MenACWY Group
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	1.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.96
upper limit	1.85

Statistical analysis title	Statistical analysis 8
Statistical analysis description: Between-group Geometric Mean Ratios (GMRs) Against N. Meningitidis Serogroup B, NZ98/254.	
Comparison groups	Naive Group v MenACWY Group
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	0.94

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	1.25

Statistical analysis title	Statistical analysis 9
Statistical analysis description:	
Between-group Geometric Mean Ratios (GMRs) Against N. Meningitidis Serogroup B, NZ98/254.	
Comparison groups	MenABCWY+OMV Group v Naive Group
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	1.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.91
upper limit	1.72

Statistical analysis title	Statistical analysis 10
Statistical analysis description:	
Between-group Geometric Mean Ratios (GMRs) Against N. Meningitidis Serogroup B, M10713.	
Comparison groups	MenABCWY+OMV Group v MenACWY Group
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	1.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.81
upper limit	2.53

Statistical analysis title	Statistical analysis 11
Statistical analysis description:	
Between-group Geometric Mean Ratios (GMRs) Against N. Meningitidis Serogroup B, M10713.	
Comparison groups	Naive Group v MenACWY Group

Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	0.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.49
upper limit	1.37

Statistical analysis title	Statistical analysis 12
Statistical analysis description:	
Between-group Geometric Mean Ratios (GMRs) Against N. Meningitidis Serogroup B, M10713.	
Comparison groups	MenABCWY+OMV Group v Naive Group
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	1.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.67
upper limit	2.06

Statistical analysis title	Statistical analysis 13
Statistical analysis description:	
Between-group Geometric Mean Ratios (GMRs) Against N. Meningitidis Serogroup B, H44/76.	
Comparison groups	MenABCWY+OMV Group v MenACWY Group
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	1.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.33
upper limit	2.78

Statistical analysis title	Statistical analysis 14
Statistical analysis description: Between-group Geometric Mean Ratios (GMRs) Against N. Meningitidis Serogroup B, H44/76.	
Comparison groups	Naive Group v MenACWY Group
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	0.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.61
upper limit	1.17

Statistical analysis title	Statistical analysis 15
Statistical analysis description: Between-group Geometric Mean Ratios (GMRs) Against N. Meningitidis Serogroup B, H44/76.	
Comparison groups	MenABCWY+OMV Group v Naive Group
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	1.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.13
upper limit	2.32

Statistical analysis title	Statistical analysis 16
Statistical analysis description: Between-group Geometric Mean Ratios (GMRs) Against N. Meningitidis Serogroup B, 5/99.	
Comparison groups	MenABCWY+OMV Group v MenACWY Group
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	7.15

Confidence interval	
level	95 %
sides	2-sided
lower limit	4.25
upper limit	12

Statistical analysis title	Statistical analysis 17
Statistical analysis description:	
Between-group Geometric Mean Ratios (GMRs) Against N. Meningitidis Serogroup B, 5/99.	
Comparison groups	Naive Group v MenACWY Group
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	0.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.59
upper limit	1.5

Statistical analysis title	Statistical analysis 18
Statistical analysis description:	
Between-group Geometric Mean Ratios (GMRs) Against N. Meningitidis Serogroup B, 5/99.	
Comparison groups	MenABCWY+OMV Group v Naive Group
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	6.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.03
upper limit	11

Statistical analysis title	Statistical analysis 19
Statistical analysis description:	
Between-group Geometric Mean Ratios (GMRs) Against N. Meningitidis Serogroup A.	
Comparison groups	MenABCWY+OMV Group v MenACWY Group

Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	0.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3
upper limit	1.23

Statistical analysis title	Statistical analysis 20
Statistical analysis description:	
Between-group Geometric Mean Ratios (GMRs) Against N. Meningitidis Serogroup A.	
Comparison groups	Naive Group v MenACWY Group
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	5.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.96
upper limit	10

Statistical analysis title	Statistical analysis 21
Statistical analysis description:	
Between-group Geometric Mean Ratios (GMRs) Against N. Meningitidis Serogroup A.	
Comparison groups	MenABCWY+OMV Group v Naive Group
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	3.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.7
upper limit	6.73

Statistical analysis title	Statistical analysis 22
Statistical analysis description:	
Between-group Geometric Mean Ratios (GMRs) Against N. Meningitidis Serogroup C.	
Comparison groups	MenABCWY+OMV Group v MenACWY Group
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	2.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.2
upper limit	5.54

Statistical analysis title	Statistical analysis 23
Statistical analysis description:	
Between-group Geometric Mean Ratios (GMRs) Against N. Meningitidis Serogroup C.	
Comparison groups	Naive Group v MenACWY Group
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.66
upper limit	2.56

Statistical analysis title	Statistical analysis 24
Statistical analysis description:	
Between-group Geometric Mean Ratios (GMRs) Against N. Meningitidis Serogroup C.	
Comparison groups	MenABCWY+OMV Group v Naive Group
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	3.34

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.57
upper limit	7.11

Statistical analysis title	Statistical analysis 25
Statistical analysis description:	
Between-group Geometric Mean Ratios (GMRs) Against N. Meningitidis Serogroup W.	
Comparison groups	MenABCWY+OMV Group v MenACWY Group
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	1.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.51
upper limit	2.59

Statistical analysis title	Statistical analysis 26
Statistical analysis description:	
Between-group Geometric Mean Ratios (GMRs) Against N. Meningitidis Serogroup W.	
Comparison groups	Naive Group v MenACWY Group
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	2.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.4
upper limit	6.12

Statistical analysis title	Statistical analysis 27
Statistical analysis description:	
Between-group Geometric Mean Ratios (GMRs) Against N. Meningitidis Serogroup W.	
Comparison groups	MenABCWY+OMV Group v Naive Group

Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	3.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.49
upper limit	7.57

Statistical analysis title	Statistical analysis 28
Statistical analysis description:	
Between-group Geometric Mean Ratios (GMRs) Against N. Meningitidis Serogroup Y.	
Comparison groups	MenABCWY+OMV Group v MenACWY Group
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	0.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.23
upper limit	1.18

Statistical analysis title	Statistical analysis 29
Statistical analysis description:	
Between-group Geometric Mean Ratios (GMRs) Against N. Meningitidis Serogroup Y.	
Comparison groups	Naive Group v MenACWY Group
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	5.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.84
upper limit	12

Statistical analysis title	Statistical analysis 30
Statistical analysis description:	
Between-group Geometric Mean Ratios (GMRs) Against N. Meningitidis Serogroup Y.	
Comparison groups	MenABCWY+OMV Group v Naive Group
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	3.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.38
upper limit	6.92

Primary: Percentages of Subjects with hSBA ≥ LLQ against N. meningitidis serogroups A, C, W and Y and B test strains.

End point title	Percentages of Subjects with hSBA ≥ LLQ against N. meningitidis serogroups A, C, W and Y and B test strains.[7]

End point description:

The HT-hSBA assay format was changed in 2015 in response to CBER comments & validation of this new format & determination of the LLOQ values for the same, are ongoing. However, the old assay format was used for sample testing in this extension trial, to maintain data comparability with the parent trials. The LLOQ cut-off values for the old assay format correspond to 8 for ACWY serogroups & 5 for B strains, & this data is already available & included in the submission. The ongoing validation procedure & determination of new LLOQ values are pertinent to the new assay format for HT-hSBA & are not considered relevant to the data obtained from the testing of the V102_02E2 study. Therefore, in the Company's judgment, the results generated with pre-defined LLOQs of 8 (for ACWY) & 5 (for B strains) are final & there will be no additional data generation with new HT-hSBA LLOQ cut-offs.

End point type	Primary

End point timeframe:

At Day 31

Notes:

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

End point values	MenABCWY+OMV Group	MenACWY Group	Naive Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[8]	0[9]	0[10]	
Units: Percentages of subjects				
number (confidence interval 95%)	(to)	(to)	(to)	

Notes:

[8] - No additional data generation with new HT-hSBA LLOQ cut-offs

[9] - No additional data generation with new HT-hSBA LLOQ cut-offs

[10] - No additional data generation with new HT-hSBA LLOQ cut-offs

Statistical analyses

No statistical analyses for this end point

Primary: Percentages of Subjects with hSBA ≥ 8 against N. meningitidis serogroups A, C, W and Y.

End point title	Percentages of Subjects with hSBA ≥ 8 against N. meningitidis serogroups A, C, W and Y.[11]

End point description:

Immune response against N. meningitidis serogroups A, C, W and Y 30 days after a single dose of MenABCWY+OMV in subjects who previously vaccinated subjects, and in Naïve subjects of similar age, as measured by the percentages of subjects with hSBA ≥ 8.
The analysis was performed on FAS immunogenicity persistence population set Day 31, which included all subjects in the Enrolled population who received a study vaccination, provided at least one evaluable serum sample at 1 month post vaccination and whose assay results were available for at least one strain.

End point type	Primary

End point timeframe:

At Day 31

Notes:

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

End point values	MenABCWY+OMV Group	MenACWY Group	Naive Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	46	50	
Units: Percentage of Subjects				
number (confidence interval 95%)				
Serogroup A (N=33;46;50)	100 (89.4 to 100.0)	100 (92.3 to 100.0)	76 (61.8 to 86.9)	
Serogroup C (N=30;38;48)	100 (88.4 to 100.0)	100 (90.7 to 100.0)	94 (82.8 to 98.7)	
Serogroup W (N=28;38;46)	100 (87.7 to 100.0)	100 (90.7 to 100.0)	96 (85.2 to 99.5)	
Serogroup Y (N=23;23;46)	100 (85.2 to 100.0)	100 (85.2 to 100.0)	85 (71.1 to 93.7)	

Statistical analyses

No statistical analyses for this end point

Primary: Percentages of Subjects with hSBA ≥ 5 against N. meningitidis serogroup B test strains.

End point title	Percentages of Subjects with hSBA ≥ 5 against N. meningitidis serogroup B test strains.[12]

End point description:

Immune response against N. meningitidis serogroup B test strains 30 days after a single dose of MenABCWY+OMV in previously vaccinated subjects, and in Naïve subjects of similar age, as measured by the percentages of Subjects with hSBA ≥ 5. The Meningococcal B Strains were M14459, M01-0240364, NZ98/254, M10713, H44/76 and 5/99.
The analysis was performed on FAS immunogenicity persistence population set Day 31, which included all subjects in the Enrolled population who received a study vaccination, provided at least one evaluable serum sample at 1 month post vaccination and whose assay results were available for at least one strain.

End point type	Primary

End point timeframe:

At Day 31

Notes:

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

End point values	MenABCWY+OMV Group	MenACWY Group	Naive Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	46	50	
Units: Percentages of Subjects				
number (confidence interval 95%)				
Serogroup B, M14459 (N=33;45;50)	85 (68.1 to 94.9)	31 (18.2 to 46.6)	40 (26.4 to 54.8)	
Serogroup B, M01-0240364 (N=30;44;45)	97 (82.8 to 99.92)	25 (13.2 to 40.3)	29 (16.4 to 44.3)	
Serogroup B, NZ98/254 (N=33;46;50)	82 (64.5 to 93.0)	37 (23.2 to 52.5)	52 (37.4 to 66.3)	
Serogroup B, M10713 (N=33;46;50)	85 (68.1 to 94.9)	52 (36.9 to 67.1)	58 (43.2 to 71.8)	
Serogroup B, H44/76 (N=33;46;50)	97 (84.2 to 99.92)	52 (36.9 to 67.1)	60 (45.2 to 73.6)	
Serogroup B, 5/99 (N=33;46;50)	100 (89.4 to 100.0)	78 (63.6 to 89.1)	82 (68.6 to 91.4)	

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean hSBA Titers (GMTs) against N. meningitidis serogroups A, C, W and Y and serogroup B test strains.

End point title	Geometric Mean hSBA Titers (GMTs) against N. meningitidis serogroups A, C, W and Y and serogroup B test strains.

End point description:

GMTs against N. meningitidis serogroups A, C, W and Y and serogroup B test strains 30 days after a single dose of MenABCWY+OMV in previously vaccinated subjects, and in Naïve subjects of similar age. The Meningococcal B Strains were M14459, M01-0240364, NZ98/254, M10713, H44/76 and 5/99. The analysis was performed on FAS immunogenicity persistence population set Day 31, which included all subjects in the Enrolled population who received a study vaccination, provided at least one evaluable serum sample at 1 month post vaccination and whose assay results were available for at least one strain.

End point type	Primary

End point timeframe:

At Day 31

End point values	MenABCWY+OMV Group	MenACWY Group	Naive Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	46	50	
Units: Titers				
geometric mean (confidence interval 95%)				
Serogroup B, M14459 (N=33;45;50)	24 (14 to 42)	2.83 (1.88 to 4.24)	4.02 (2.67 to 6.06)	
Serogroup B, M01-0240364 (N=30;44;45)	601 (339 to 1064)	3.05 (1.77 to 5.26)	3.11 (1.76 to 5.51)	
Serogroup B, NZ98/254 (N=33;46;50)	13 (8.50 to 18)	3.57 (2.37 to 5.38)	5.75 (3.95 to 8.37)	
Serogroup B, M10713 (N=33;46;50)	20 (13 to 31)	5.51 (3.45 to 8.79)	7.70 (5.04 to 12)	
Serogroup B, H44/76 (N=33;46;50)	98 (57 to 170)	5.78 (3.59 to 9.31)	7.27 (4.53 to 12)	
Serogroup B, 5/99 (N=33;46;50)	1426 (940 to 2164)	19 (11 to 34)	25 (15 to 42)	
Serogroup A (N=33;46;50)	396 (288 to 545)	149 (106 to 210)	22 (14 to 35)	
Serogroup C (N=30;38;48)	1676 (1164 to 2414)	1199 (849 to 1692)	58 (35 to 96)	
Serogroup W (N=28;38;46)	1823 (1163 to 2856)	2259 (1678 to 3041)	117 (83 to 166)	
Serogroup Y (N=23;23;46)	779 (430 to 1413)	1692 (1206 to 2373)	85 (45 to 163)	

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description: Between-group Geometric Mean Ratios (GMRs) Against N. Meningitidis Serogroup B, M14459.	
Comparison groups	MenABCWY+OMV Group v MenACWY Group
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	8.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.41
upper limit	16

Statistical analysis title	Statistical analysis 2
Statistical analysis description: Between-group Geometric Mean Ratios (GMRs) Against N. Meningitidis Serogroup B, M14459.	
Comparison groups	Naive Group v MenACWY Group

Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.39
upper limit	1.27

Statistical analysis title	Statistical analysis 3
Statistical analysis description:	
Between-group Geometric Mean Ratios (GMRs) Against N. Meningitidis Serogroup B, M14459.	
Comparison groups	Naive Group v MenABCWY+OMV Group
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	5.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.14
upper limit	11

Statistical analysis title	Statistical analysis 4
Statistical analysis description:	
Between-group Geometric Mean Ratios (GMRs) Against N. Meningitidis Serogroup B, M01-0240364.	
Comparison groups	MenABCWY+OMV Group v MenACWY Group
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	197
Confidence interval	
level	95 %
sides	2-sided
lower limit	86
upper limit	452

Statistical analysis title	Statistical analysis 5
Statistical analysis description: Between-group Geometric Mean Ratios (GMRs) Against N. Meningitidis Serogroup B, M01-0240364.	
Comparison groups	Naive Group v MenACWY Group
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	0.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.47
upper limit	2.07

Statistical analysis title	Statistical analysis 6
Statistical analysis description: Between-group Geometric Mean Ratios (GMRs) Against N. Meningitidis Serogroup B, M01-0240364.	
Comparison groups	Naive Group v MenABCWY+OMV Group
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	193
Confidence interval	
level	95 %
sides	2-sided
lower limit	84
upper limit	442

Statistical analysis title	Statistical analysis 7
Statistical analysis description: Between-group Geometric Mean Ratios (GMRs) Against N. Meningitidis Serogroup B, NZ98/254.	
Comparison groups	MenABCWY+OMV Group v MenACWY Group
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	3.51

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.96
upper limit	6.27

Statistical analysis title	Statistical analysis 8
Statistical analysis description:	
Between-group Geometric Mean Ratios (GMRs) Against N. Meningitidis Serogroup B, NZ98/254.	
Comparison groups	Naive Group v MenACWY Group
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	other
Method	Mixed models analysis
Parameter estimate	Geometric mean ratio
Point estimate	0.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.37
upper limit	1

Statistical analysis title	Statistical analysis 9
Statistical analysis description:	
Between-group Geometric Mean Ratios (GMRs) Against N. Meningitidis Serogroup B, NZ98/254.	
Comparison groups	Naive Group v MenABCWY+OMV Group
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	2.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.23
upper limit	3.85

Statistical analysis title	Statistical analysis 10
Statistical analysis description:	
Between-group Geometric Mean Ratios (GMRs) Against N. Meningitidis Serogroup B, M10713.	
Comparison groups	MenABCWY+OMV Group v MenACWY Group

Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	3.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.84
upper limit	6.92

Statistical analysis title	Statistical analysis 11
Statistical analysis description: Between-group Geometric Mean Ratios (GMRs) Against N. Meningitidis Serogroup B, M10713.	
Comparison groups	Naive Group v MenACWY Group
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	0.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.4
upper limit	1.29

Statistical analysis title	Statistical analysis 12
Statistical analysis description: Between-group Geometric Mean Ratios (GMRs) Against N. Meningitidis Serogroup B, M10713.	
Comparison groups	Naive Group v MenABCWY+OMV Group
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	2.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.33
upper limit	4.89

Statistical analysis title	Statistical analysis 13
Statistical analysis description: Between-group Geometric Mean Ratios (GMRs) Against N. Meningitidis Serogroup B, H44/76.	
Comparison groups	MenABCWY+OMV Group v MenACWY Group
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	17
Confidence interval	
level	95 %
sides	2-sided
lower limit	8.18
upper limit	35

Statistical analysis title	Statistical analysis 14
Statistical analysis description: Between-group Geometric Mean Ratios (GMRs) Against N. Meningitidis Serogroup B, H44/76.	
Comparison groups	Naive Group v MenACWY Group
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.41
upper limit	1.53

Statistical analysis title	Statistical analysis 15
Statistical analysis description: Between-group Geometric Mean Ratios (GMRs) Against N. Meningitidis Serogroup B, H44/76.	
Comparison groups	Naive Group v MenABCWY+OMV Group
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	13

Confidence interval	
level	95 %
sides	2-sided
lower limit	6.59
upper limit	28

Statistical analysis title	Statistical analysis 16
Statistical analysis description:	
Between-group Geometric Mean Ratios (GMRs) Against N. Meningitidis Serogroup B, 5/99.	
Comparison groups	MenABCWY+OMV Group v MenACWY Group
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	74
Confidence interval	
level	95 %
sides	2-sided
lower limit	34
upper limit	160

Statistical analysis title	Statistical analysis 17
Statistical analysis description:	
Between-group Geometric Mean Ratios (GMRs) Against N. Meningitidis Serogroup B, 5/99.	
Comparison groups	Naive Group v MenACWY Group
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	0.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.38
upper limit	1.53

Statistical analysis title	Statistical analysis 18
Statistical analysis description:	
Between-group Geometric Mean Ratios (GMRs) Against N. Meningitidis Serogroup B, 5/99.	
Comparison groups	Naive Group v MenABCWY+OMV Group

Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	57
Confidence interval	
level	95 %
sides	2-sided
lower limit	27
upper limit	121

Statistical analysis title	Statistical analysis 19
Statistical analysis description:	
Between-group Geometric Mean Ratios (GMRs) Against N. Meningitidis Serogroup A.	
Comparison groups	MenABCWY+OMV Group v MenACWY Group
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	2.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.46
upper limit	4.83

Statistical analysis title	Statistical analysis 20
Statistical analysis description:	
Between-group Geometric Mean Ratios (GMRs) Against N. Meningitidis Serogroup A.	
Comparison groups	Naive Group v MenACWY Group
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	6.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.96
upper limit	12

Statistical analysis title	Statistical analysis 21
Statistical analysis description:	
Between-group Geometric Mean Ratios (GMRs) Against N. Meningitidis Serogroup A.	
Comparison groups	Naive Group v MenABCWY+OMV Group
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	18
Confidence interval	
level	95 %
sides	2-sided
lower limit	10
upper limit	32

Statistical analysis title	Statistical analysis 22
Statistical analysis description:	
Between-group Geometric Mean Ratios (GMRs) Against N. Meningitidis Serogroup C.	
Comparison groups	MenABCWY+OMV Group v MenACWY Group
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.72
upper limit	2.71

Statistical analysis title	Statistical analysis 23
Statistical analysis description:	
Between-group Geometric Mean Ratios (GMRs) Against N. Meningitidis Serogroup C.	
Comparison groups	Naive Group v MenACWY Group
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	21

Confidence interval	
level	95 %
sides	2-sided
lower limit	12
upper limit	37

Statistical analysis title	Statistical analysis 24
Statistical analysis description:	
Between-group Geometric Mean Ratios (GMRs) Against N. Meningitidis Serogroup C.	
Comparison groups	Naive Group v MenABCWY+OMV Group
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	29
Confidence interval	
level	95 %
sides	2-sided
lower limit	15
upper limit	55

Statistical analysis title	Statistical analysis 25
Statistical analysis description:	
Between-group Geometric Mean Ratios (GMRs) Against N. Meningitidis Serogroup W.	
Comparison groups	MenABCWY+OMV Group v MenACWY Group
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	0.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.47
upper limit	1.38

Statistical analysis title	Statistical analysis 26
Statistical analysis description:	
Between-group Geometric Mean Ratios (GMRs) Against N. Meningitidis Serogroup W.	
Comparison groups	Naive Group v MenACWY Group

Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	19
Confidence interval	
level	95 %
sides	2-sided
lower limit	12
upper limit	31

Statistical analysis title	Statistical analysis 27
Statistical analysis description:	
Between-group Geometric Mean Ratios (GMRs) Against N. Meningitidis Serogroup W.	
Comparison groups	Naive Group v MenABCWY+OMV Group
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	16
Confidence interval	
level	95 %
sides	2-sided
lower limit	9.27
upper limit	26

Statistical analysis title	Statistical analysis 28
Statistical analysis description:	
Between-group Geometric Mean Ratios (GMRs) Against N. Meningitidis Serogroup Y.	
Comparison groups	MenABCWY+OMV Group v MenACWY Group
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	0.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.17
upper limit	1.28

Statistical analysis title	Statistical analysis 29
Statistical analysis description:	
Between-group Geometric Mean Ratios (GMRs) Against N. Meningitidis Serogroup Y.	
Comparison groups	Naive Group v MenACWY Group
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	20
Confidence interval	
level	95 %
sides	2-sided
lower limit	8.2
upper limit	48

Statistical analysis title	Statistical analysis 30
Statistical analysis description:	
Between-group Geometric Mean Ratios (GMRs) Against N. Meningitidis Serogroup Y.	
Comparison groups	Naive Group v MenABCWY+OMV Group
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	9.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.78
upper limit	22

Primary: Geometric Mean hSBA Ratio (GMRs) against N. meningitidis serogroups A, C, W and Y and serogroup B test strains.

End point title	Geometric Mean hSBA Ratio (GMRs) against N. meningitidis serogroups A, C, W and Y and serogroup B test strains.[13]

End point description:

GMRs as measure of the immune response against N. meningitidis serogroups A, C, W and Y and serogroup B test strains in previously vaccinated subjects, and in Naïve subjects of similar age. The Meningococcal B Strains were M14459, M01-0240364, NZ98/254, M10713, H44/76 and 5/99.
The analysis was performed on FAS immunogenicity persistence population set Day 31, which included all subjects in the Enrolled population who received a study vaccination, provided at least one evaluable serum sample at 1 month post vaccination and whose assay results were available for at least one strain.

End point type	Primary

End point timeframe:

Day 31 versus Day 1

Notes:

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

End point values	MenABCWY+OMV Group	MenACWY Group	Naive Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	46	50	
Units: Ratios				
geometric mean (confidence interval 95%)				
Serogroup B, M14459 (N=33;45;50)	12 (6.88 to 20)	2.11 (1.45 to 3.07)	2.72 (1.91 to 3.87)	
Serogroup B, M01-0240364 (N=28;42;45)	229 (108 to 485)	2.80 (1.59 to 4.96)	2.48 (1.51 to 4.07)	
Serogroup B, NZ98/254 (N=33;46;50)	6.92 (4.61 to 10)	2.64 (1.73 to 4.02)	3.98 (2.73 to 5.79)	
Serogroup B, M10713 (N=33;46;50)	5.38 (3.54 to 8.17)	2.15 (1.46 to 3.17)	2.48 (1.78 to 3.45)	
Serogroup B, H44/76 (N=33;46;50)	42 (25 to 72)	4.78 (2.90 to 7.89)	5.06 (3.21 to 7.97)	
Serogroup B, 5/99 (N=33;46;50)	112 (68 to 185)	11 (6.09 to 19)	13 (8.14 to 22)	
Serogroup A (N=33;46;50)	98 (54 to 177)	22 (13 to 38)	18 (12 to 29)	
Serogroup C (N=30;38;48)	105 (49 to 222)	238 (145 to 392)	12 (6.88 to 19)	
Serogroup W (N=28;38;44)	67 (34 to 132)	112 (65 to 191)	16 (8.35 to 30)	
Serogroup Y (N=22;22;43)	162 (70 to 375)	216 (80 to 580)	46 (23 to 92)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentages of Subjects with hSBA ≥ LLQ against N. meningitidis serogroups A, C, W and Y and serogroup B test strains.

End point title	Percentages of Subjects with hSBA ≥ LLQ against N. meningitidis serogroups A, C, W and Y and serogroup B test strains.

End point description:

The HT-hSBA assay format was changed in 2015 in response to CBER comments & validation of this new format & determination of the LLOQ values for the same, are ongoing. However, the old assay format was used for sample testing in this extension trial, to maintain data comparability with the parent trials. The LLOQ cut-off values for the old assay format correspond to 8 for ACWY serogroups & 5 for B strains, & this data is already available & included in the submission. The ongoing validation procedure & determination of new LLOQ values are pertinent to the new assay format for HT-hSBA & are not considered relevant to the data obtained from the testing of the V102_02E2 study. Therefore, in the Company's judgment, the results generated with pre-defined LLOQs of 8 (for ACWY) & 5 (for B strains) are final & there will be no additional data generation with new HT-hSBA LLOQ cut-offs.

End point type	Secondary

End point timeframe:

At Days 1, 4, 8 and 31

End point values	MenABCWY+OMV Group	MenACWY Group	Naive Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[14]	0[15]	0[16]	
Units: Percentages of subjects				
number (confidence interval 95%)	(to)	(to)	(to)	

Notes:

[14] - No additional data generation with new HT-hSBA LLOQ cut-offs

[15] - No additional data generation with new HT-hSBA LLOQ cut-offs

[16] - No additional data generation with new HT-hSBA LLOQ cut-offs

Statistical analyses

No statistical analyses for this end point

Secondary: Percentages of Subjects with hSBA ≥ LLQ against N. meningitidis serogroups A, C, W and Y and serogroup B test strains.

End point title	Percentages of Subjects with hSBA ≥ LLQ against N. meningitidis serogroups A, C, W and Y and serogroup B test strains.

End point description:

The HT-hSBA assay format was changed in 2015 in response to CBER comments & validation of this new format & determination of the LLOQ values for the same, are ongoing. However, the old assay format was used for sample testing in this extension trial, to maintain data comparability with the parent trials. The LLOQ cut-off values for the old assay format correspond to 8 for ACWY serogroups & 5 for B strains, & this data is already available & included in the submission. The ongoing validation procedure & determination of new LLOQ values are pertinent to the new assay format for HT-hSBA & are not considered relevant to the data obtained from the testing of the V102_02E2 study. Therefore, in the Company's judgment, the results generated with pre-defined LLOQs of 8 (for ACWY) & 5 (for B strains) are final & there will be no additional data generation with new HT-hSBA LLOQ cut-offs.

End point type	Secondary

End point timeframe:

At Days 1, 31, 34, 38 and 61

End point values	MenABCWY+OMV Group	MenACWY Group	Naive Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[17]	0[18]	0[19]	
Units: Percentage of subjects				
number (confidence interval 95%)	(to)	(to)	(to)	

Notes:

[17] - No additional data generation with new HT-hSBA LLOQ cut-offs

[18] - No additional data generation with new HT-hSBA LLOQ cut-offs

[19] - No additional data generation with new HT-hSBA LLOQ cut-offs

Statistical analyses

No statistical analyses for this end point

Secondary: Percentages of Subjects with hSBA ≥ 8 against N. meningitidis serogroups A, C, W and Y.

End point title	Percentages of Subjects with hSBA ≥ 8 against N. meningitidis serogroups A, C, W and Y.

End point description:

Kinetics of immune response following 1 dose of MenABCWY+OMV in subjects who previously received 2 doses of MenABCWY+OMV or 1 dose of MenACWY, at Days 1, 4, 8, 31, 34, 38 and 61, as measured by the percentages of subjects with hSBA ≥ 8.
The analysis was performed on FAS immunogenicity kinetics population set, which included all subjects in the Enrolled population who received a study vaccination, provided at least one evaluable serum sample post vaccination and whose assay results were available for at least one strain.

End point type	Secondary

End point timeframe:

At Days 1, 4, 8, 31, 34, 38 and 61

End point values	MenABCWY+OMV Group (A)	MenACWY Group (B1)	MenACWY group (B2)	Naive Group (C1)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	33	23	23	26
Units: Percentages of subjects				
number (confidence interval 95%)				
Serogroup A; Day 1 (N=33;23;23;26;24)	27 (13.3 to 45.5)	52 (30.6 to 73.2)	30 (13.2 to 52.9)	0 (0.0 to 13.2)
Serogroup A; Day 4 (N=33;23;0;0;0)	24 (11.1 to 42.3)	52 (30.6 to 73.2)	0 (0 to 0)	0 (0 to 0)
Serogroup A; Day 8 (N=33;0;22;0;0)	100 (89.4 to 100.0)	0 (0 to 0)	82 (59.7 to 94.8)	0 (0 to 0)
Serogroup A; Day 31 (N=33;23;23;26;24)	100 (89.4 to 100.0)	100 (85.2 to 100.0)	100 (85.2 to 100.0)	73 (52.2 to 88.4)
Serogroup A; Day 34 (N=0;0;0;26;0)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	77 (56.4 to 91.0)
Serogroup A; Day 38 (N=0;0;0;0;24)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)
Serogroup A; Day 61 (N=0;23;23;23;24)	0 (0 to 0)	100 (85.2 to 100.0)	100 (85.2 to 100.0)	100 (85.2 to 100.0)
Serogroup C; Day 1 (N=32;23;23;25;24)	69 (50.0 to 83.9)	61 (38.5 to 80.3)	26 (10.2 to 48.4)	40 (21.1 to 61.3)
Serogroup C; Day 4 (N=30;22;0;0;0)	73 (54.1 to 87.7)	64 (40.7 to 82.8)	0 (0 to 0)	0 (0 to 0)
Serogroup C; Day 8 (N=29;0;19;0;0)	100 (88.1 to 100.0)	0 (0 to 0)	100 (82.4 to 100.0)	0 (0 to 0)
Serogroup C; Day 31 (N=30;17;21;25;23)	100 (88.4 to 100.0)	100 (80.5 to 100.0)	100 (83.9 to 100.0)	100 (86.3 to 100.0)
Serogroup C; Day 34 (N=0;0;0;20;0)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	100 (83.2 to 100.0)
Serogroup C; Day 38 (N=0;0;0;0;22)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)
Serogroup C; Day 61 (N=0;15;19;24;23)	0 (0 to 0)	100 (78.2 to 100.0)	100 (82.4 to 100.0)	100 (85.8 to 100.0)
Serogroup W; Day 1 (N=32;23;23;25;22)	75 (56.6 to 88.5)	70 (47.1 to 86.8)	87 (66.4 to 97.2)	44 (24.4 to 65.1)
Serogroup W; Day 4 (N=25;22;0;0;0)	76 (54.9 to 90.6)	73 (49.8 to 89.3)	0 (0 to 0)	0 (0 to 0)
Serogroup W; Day 8 (N=25;0;16;0;0)	100 (86.3 to 100.0)	0 (0 to 0)	100 (79.4 to 100.0)	0 (0 to 0)
Serogroup W; Day 31 (N=28;17;21;22;24)	100 (87.7 to 100.0)	100 (80.5 to 100.0)	100 (83.9 to 100.0)	100 (84.6 to 100.0)

Serogroup W; Day 34 (N=0;0;0;19;0)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	100 (82.4 to 100.0)
Serogroup W; Day 38 (N=0;0;0;0;20)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)
Serogroup W; Day 61 (N=0;15;17;20;21)	0 (0 to 0)	100 (78.2 to 100.0)	100 (80.5 to 100.0)	100 (83.2 to 100.0)
Serogroup Y; Day 1 (N=32;22;22;23;24)	38 (21.1 to 56.3)	64 (40.7 to 82.8)	55 (32.2 to 75.6)	17 (5.0 to 38.8)
Serogroup Y; Day 4 (N=31;22;0;0;0)	42 (24.5 to 60.9)	50 (28.2 to 71.8)	0 (0 to 0)	0 (0 to 0)
Serogroup Y; Day 8 (N=23;0;13;0;0)	100 (85.2 to 100.0)	0 (0 to 0)	100 (75.3 to 100.0)	0 (0 to 0)
Serogroup Y; Day 31 (N=23;12;11;23;23)	100 (85.2 to 100.0)	100 (73.5 to 100.0)	100 (71.5 to 100.0)	91 (72.0 to 98.9)
Serogroup Y; Day 34 (N=0;0;0;23;0)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	96 (78.1 to 99.89)
Serogroup Y; Day 38 (N=0;0;0;0;20)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)
Serogroup Y; Day 61 (N=0;12;15;23;20)	0 (0 to 0)	100 (73.5 to 100.0)	100 (78.2 to 100.0)	100 (85.2 to 100.0)

End point values	Naive Group (C2)			
Subject group type	Subject analysis set			
Number of subjects analysed	24			
Units: Percentages of subjects				
number (confidence interval 95%)				
Serogroup A; Day 1 (N=33;23;23;26;24)	4 (0.11 to 21.1)			
Serogroup A; Day 4 (N=33;23;0;0;0)	0 (0 to 0)			
Serogroup A; Day 8 (N=33;0;22;0;0)	0 (0 to 0)			
Serogroup A; Day 31 (N=33;23;23;26;24)	79 (57.8 to 92.9)			
Serogroup A; Day 34 (N=0;0;0;26;0)	0 (0 to 0)			
Serogroup A; Day 38 (N=0;0;0;0;24)	96 (78.9 to 99.89)			
Serogroup A; Day 61 (N=0;23;23;23;24)	88 (67.6 to 97.3)			
Serogroup C; Day 1 (N=32;23;23;25;24)	50 (29.1 to 70.9)			
Serogroup C; Day 4 (N=30;22;0;0;0)	0 (0 to 0)			
Serogroup C; Day 8 (N=29;0;19;0;0)	0 (0 to 0)			
Serogroup C; Day 31 (N=30;17;21;25;23)	87 (66.4 to 97.2)			
Serogroup C; Day 34 (N=0;0;0;20;0)	0 (0 to 0)			
Serogroup C; Day 38 (N=0;0;0;0;22)	100 (84.6 to 100.0)			
Serogroup C; Day 61 (N=0;15;19;24;23)	100 (85.2 to 100.0)			
Serogroup W; Day 1 (N=32;23;23;25;22)	64 (40.7 to 82.8)			
Serogroup W; Day 4 (N=25;22;0;0;0)	0 (0 to 0)			
Serogroup W; Day 8 (N=25;0;16;0;0)	0 (0 to 0)			
Serogroup W; Day 31 (N=28;17;21;22;24)	92 (73.0 to 99.0)			
Serogroup W; Day 34 (N=0;0;0;19;0)	0 (0 to 0)			
Serogroup W; Day 38 (N=0;0;0;0;20)	100 (83.2 to 100.0)			

Serogroup W; Day 61 (N=0;15;17;20;21)	100 (83.9 to 100.0)			
Serogroup Y; Day 1 (N=32;22;22;23;24)	21 (7.1 to 42.2)			
Serogroup Y; Day 4 (N=31;22;0;0;0)	0 (0 to 0)			
Serogroup Y; Day 8 (N=23;0;13;0;0)	0 (0 to 0)			
Serogroup Y; Day 31 (N=23;12;11;23;23)	78 (56.3 to 92.5)			
Serogroup Y; Day 34 (N=0;0;0;23;0)	0 (0 to 0)			
Serogroup Y; Day 38 (N=0;0;0;0;20)	100 (83.2 to 100.0)			
Serogroup Y; Day 61 (N=0;12;15;23;20)	95 (75.1 to 99.87)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentages of Subjects with hSBA ≥ 5 against N. meningitidis serogroup B test strains.

End point title	Percentages of Subjects with hSBA ≥ 5 against N. meningitidis serogroup B test strains.

End point description:

Kinetics of immune response against N. meningitidis serogroup B test strains in previously vaccinated subjects, at Days 1, 4, 8, 31, 34, 38 and 61, as measured by the percentages of Subjects with hSBA ≥ 5. The Meningococcal B Strains were M14459, M01-0240364, NZ98/254, M10713, H44/76 and 5/99. The analysis was performed on FAS immunogenicity kinetics population set, which included all subjects in the Enrolled population who received a study vaccination, provided at least one evaluable serum sample post vaccination and whose assay results were available for at least one strain.

End point type	Secondary

End point timeframe:

At Days 1, 4, 8, 31, 34, 38 and 61

End point values	MenABCWY+OMV Group (A)	MenACWY Group (B1)	MenACWY group (B2)	Naive Group (C1)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	33	23	23	26
Units: Percentages of subjects				
number (confidence interval 95%)				
Serogroup B, M14459; Day 1 (N=33;23;23;26;24)	18 (7.0 to 35.5)	9 (1.1 to 28.0)	0 (0.0 to 14.8)	8 (0.9 to 25.1)
Serogroup B, M14459; Day 4 (N=33;23;0;0;0)	21 (9.0 to 38.9)	4 (0.11 to 21.9)	0 (0 to 0)	0 (0 to 0)
Serogroup B, M14459; Day 8 (N=33;0;22;0;0)	79 (61.1 to 91.0)	0 (0 to 0)	14 (2.9 to 34.9)	0 (0 to 0)
Serogroup B, M14459; Day 31 (N=33;23;22;26;24)	85 (68.1 to 94.9)	35 (16.4 to 57.3)	27 (10.7 to 50.2)	46 (26.6 to 66.6)
Serogroup B, M14459; Day 34 (N=0;0;0;26;0)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	42 (23.4 to 63.1)
Serogroup B, M14459; Day 38 (N=0;0;0;0;24)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)

Serogroup B, M14459; Day 61 (N=0;23;23;25;24)	0 (0 to 0)	43 (23.2 to 65.5)	48 (26.8 to 69.4)	80 (59.3 to 93.2)
Serogroup B, M01-0240364; Day 1(N=31;22;22;26;24)	13 (3.6 to 29.8)	9 (1.1 to 29.2)	0 (0.0 to 15.4)	4 (0.10 to 19.6)
Serogroup B, M01-0240364; Day 4 (N=30;23;0;0;0)	17 (5.6 to 34.7)	4 (0.11 to 21.9)	0 (0 to 0)	0 (0 to 0)
Serogroup B, M01-0240364; Day 8 (N=29;0;21;0;0)	93 (77.2 to 99.2)	0 (0 to 0)	10 (1.2 to 30.4)	0 (0 to 0)
Serogroup B, M01-0240364;Day 31(N=30;21;23;24;21)	97 (82.8 to 99.92)	29 (11.3 to 52.2)	22 (7.5 to 43.7)	33 (15.6 to 55.3)
Serogroup B, M01-0240364; Day 34 (N=0;0;0;25;0)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	40 (21.1 to 61.3)
Serogroup B, M01-0240364; Day 38 (N=0;0;0;0;22)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)
Serogroup B, M01-0240364; Day 61(N=0;23;23;23;24)	0 (0 to 0)	65 (42.7 to 83.6)	65 (42.7 to 83.6)	70 (47.1 to 86.8)
Serogroup B, NZ98/254; Day 1 (N=33;23;23;26;24)	15 (5.1 to 31.9)	4 (0.11 to 21.9)	0 (0.0 to 14.8)	8 (0.9 to 25.1)
Serogroup B, NZ98/254; Day 4 (N=33;23;0;0;0)	12 (3.4 to 28.2)	13 (2.8 to 33.6)	0 (0 to 0)	0 (0 to 0)
Serogroup B, NZ98/254; Day 8 (N=33;0;22;0;0)	67 (48.2 to 82.0)	0 (0 to 0)	9 (1.1 to 29.2)	0 (0 to 0)
Serogroup B, NZ98/254; Day 31 (N=33;23;23;26;24)	82 (64.5 to 93.0)	48 (26.8 to 69.4)	26 (10.2 to 48.4)	58 (36.9 to 76.6)
Serogroup B, NZ98/254; Day 34 (N=0;0;0;26;0)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	50 (29.9 to 70.1)
Serogroup B, NZ98/254; Day 38 (N=0;0;0;0;24)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)
Serogroup B, NZ98/254; Day 61 (N=0;23;23;25;24)	0 (0 to 0)	52 (30.6 to 73.2)	39 (19.7 to 61.5)	72 (50.6 to 87.9)
Serogroup B, M10713; Day 1 (N=33;23;23;26;24)	48 (30.8 to 66.5)	48 (26.8 to 69.4)	17 (5.0 to 38.8)	38 (20.2 to 59.4)
Serogroup B, M10713; Day 4 (N=32;23;0;0;0)	56 (37.7 to 73.6)	39 (19.7 to 61.5)	0 (0 to 0)	0 (0 to 0)
Serogroup B, M10713; Day 8 (N=33;0;22;0;0)	79 (61.1 to 91.0)	0 (0 to 0)	32 (13.9 to 54.9)	0 (0 to 0)
Serogroup B, M10713; Day 31 (N=33;23;23;26;24)	85 (68.1 to 94.9)	70 (47.1 to 86.8)	35 (16.4 to 57.3)	62 (40.6 to 79.8)
Serogroup B, M10713; Day 34 (N=0;0;0;23;0)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	57 (34.5 to 76.8)
Serogroup B, M10713; Day 38 (N=0;0;0;0;24)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)
Serogroup B, M10713; Day 61 (N=0;23;23;25;24)	0 (0 to 0)	65 (42.7 to 83.6)	43 (23.2 to 65.5)	68 (46.5 to 85.1)
Serogroup B, H44/76; Day 1 (N=33;23;23;26;24)	27 (13.3 to 45.5)	9 (1.1 to 28.0)	0 (0.0 to 14.8)	12 (2.4 to 30.2)
Serogroup B, H44/76; Day 4 (N=33;23;0;0;0)	21 (9.0 to 38.9)	4 (0.11 to 21.9)	0 (0 to 0)	0 (0 to 0)
Serogroup B, H44/76; Day 8 (N=33;0;22;0;0)	94 (79.8 to 99.3)	0 (0 to 0)	14 (2.9 to 34.9)	0 (0 to 0)
Serogroup B, H44/76; Day 31 (N=33;23;23;26;24)	97 (84.2 to 99.92)	52 (30.6 to 73.2)	52 (30.6 to 73.2)	73 (52.2 to 88.4)
Serogroup B, H44/76; Day 34 (N=0;0;0;26;0)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	69 (48.2 to 85.7)
Serogroup B, H44/76; Day 38 (N=0;0;0;0;24)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)
Serogroup B, H44/76; Day 61 (N=0;23;23;25;24)	0 (0 to 0)	78 (56.3 to 92.5)	91 (72.0 to 98.9)	96 (79.6 to 99.90)
Serogroup B, 5/99; Day 1 (N=33;23;23;26;24)	70 (51.3 to 84.4)	22 (7.5 to 43.7)	13 (2.8 to 33.6)	19 (6.6 to 39.4)
Serogroup B, 5/99; Day 4 (N=33;23;0;0;0)	79 (61.1 to 91.0)	9 (1.1 to 28.0)	0 (0 to 0)	0 (0 to 0)

Serogroup B, 5/99; Day 8 (N=33;0;22;0;0)	100 (89.4 to 100.0)	0 (0 to 0)	9 (1.1 to 29.2)	0 (0 to 0)
Serogroup B, 5/99; Day 31 (N=33;23;23;26;24)	100 (89.4 to 100.0)	78 (56.3 to 92.5)	78 (56.3 to 92.5)	85 (65.1 to 95.6)
Serogroup B, 5/99; Day 34 (N=0;0;0;26;0)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	85 (65.1 to 95.6)
Serogroup B, 5/99; Day 38 (N=0;0;0;0;24)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)
Serogroup B, 5/99; Day 61 (N=0;23;23;25;24)	0 (0 to 0)	100 (85.2 to 100.0)	100 (85.2 to 100.0)	100 (86.3 to 100.0)

End point values	Naive Group (C2)			
Subject group type	Subject analysis set			
Number of subjects analysed	24			
Units: Percentages of subjects				
number (confidence interval 95%)				
Serogroup B, M14459; Day 1 (N=33;23;23;26;24)	8 (1.0 to 27.0)			
Serogroup B, M14459; Day 4 (N=33;23;0;0;0)	0 (0 to 0)			
Serogroup B, M14459; Day 8 (N=33;0;22;0;0)	0 (0 to 0)			
Serogroup B, M14459; Day 31 (N=33;23;22;26;24)	33 (15.6 to 55.3)			
Serogroup B, M14459; Day 34 (N=0;0;0;26;0)	0 (0 to 0)			
Serogroup B, M14459; Day 38 (N=0;0;0;0;24)	71 (48.9 to 87.4)			
Serogroup B, M14459; Day 61 (N=0;23;23;25;24)	54 (32.8 to 74.4)			
Serogroup B, M01-0240364; Day 1(N=31;22;22;26;24)	4 (0.11 to 21.1)			
Serogroup B, M01-0240364; Day 4 (N=30;23;0;0;0)	0 (0 to 0)			
Serogroup B, M01-0240364; Day 8 (N=29;0;21;0;0)	0 (0 to 0)			
Serogroup B, M01-0240364;Day 31(N=30;21;23;24;21)	24 (8.2 to 47.2)			
Serogroup B, M01-0240364; Day 34 (N=0;0;0;25;0)	0 (0 to 0)			
Serogroup B, M01-0240364; Day 38 (N=0;0;0;0;22)	82 (59.7 to 94.8)			
Serogroup B, M01-0240364; Day 61(N=0;23;23;23;24)	71 (48.9 to 87.4)			
Serogroup B, NZ98/254; Day 1 (N=33;23;23;26;24)	4 (0.11 to 21.1)			
Serogroup B, NZ98/254; Day 4 (N=33;23;0;0;0)	0 (0 to 0)			
Serogroup B, NZ98/254; Day 8 (N=33;0;22;0;0)	0 (0 to 0)			
Serogroup B, NZ98/254; Day 31 (N=33;23;23;26;24)	46 (25.6 to 67.2)			
Serogroup B, NZ98/254; Day 34 (N=0;0;0;26;0)	0 (0 to 0)			
Serogroup B, NZ98/254; Day 38 (N=0;0;0;0;24)	75 (53.3 to 90.2)			

Serogroup B, NZ98/254; Day 61 (N=0;23;23;25;24)	50 (29.1 to 70.9)			
Serogroup B, M10713; Day 1 (N=33;23;23;26;24)	38 (18.8 to 59.4)			
Serogroup B, M10713; Day 4 (N=32;23;0;0;0)	0 (0 to 0)			
Serogroup B, M10713; Day 8 (N=33;0;22;0;0)	0 (0 to 0)			
Serogroup B, M10713; Day 31 (N=33;23;23;26;24)	54 (32.8 to 74.4)			
Serogroup B, M10713; Day 34 (N=0;0;0;23;0)	0 (0 to 0)			
Serogroup B, M10713; Day 38 (N=0;0;0;0;24)	67 (44.7 to 84.4)			
Serogroup B, M10713; Day 61 (N=0;23;23;25;24)	63 (40.6 to 81.2)			
Serogroup B, H44/76; Day 1 (N=33;23;23;26;24)	8 (1.0 to 27.0)			
Serogroup B, H44/76; Day 4 (N=33;23;0;0;0)	0 (0 to 0)			
Serogroup B, H44/76; Day 8 (N=33;0;22;0;0)	0 (0 to 0)			
Serogroup B, H44/76; Day 31 (N=33;23;23;26;24)	46 (25.6 to 67.2)			
Serogroup B, H44/76; Day 34 (N=0;0;0;26;0)	0 (0 to 0)			
Serogroup B, H44/76; Day 38 (N=0;0;0;0;24)	96 (78.9 to 99.89)			
Serogroup B, H44/76; Day 61 (N=0;23;23;25;24)	79 (57.8 to 92.9)			
Serogroup B, 5/99; Day 1 (N=33;23;23;26;24)	13 (2.7 to 32.4)			
Serogroup B, 5/99; Day 4 (N=33;23;0;0;0)	0 (0 to 0)			
Serogroup B, 5/99; Day 8 (N=33;0;22;0;0)	0 (0 to 0)			
Serogroup B, 5/99; Day 31 (N=33;23;23;26;24)	79 (57.8 to 92.9)			
Serogroup B, 5/99; Day 34 (N=0;0;0;26;0)	0 (0 to 0)			
Serogroup B, 5/99; Day 38 (N=0;0;0;0;24)	100 (85.8 to 100.0)			
Serogroup B, 5/99; Day 61 (N=0;23;23;25;24)	100 (85.8 to 100.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean hSBA Titers (GMTs) against N. meningitidis serogroups A, C, W and Y and serogroup B test strains.

End point title	Geometric Mean hSBA Titers (GMTs) against N. meningitidis serogroups A, C, W and Y and serogroup B test strains.[20]

End point description:

GMTs at Day 1, 4, 8, 31 as measure of the kinetics of the immune response following a dose of MenABCWY+OMV, in subjects who previously received 2 doses of MenABCWY+OMV or 1 dose of MenACWY. This outcome measure reports data only for the MenABCWY+OMV and MenACWY Groups as per protocol. The Meningococcal B Strains were M14459, M01-0240364, NZ98/254, M10713, H44/76

and 5/99.
The analysis was performed on FAS immunogenicity kinetics population set, which included all subjects in the Enrolled population who received a study vaccination, provided at least one evaluable serum sample post vaccination and whose assay results were available for at least one strain.

End point type	Secondary

End point timeframe:

At Days 1, 4, 8 and 31

Notes:

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

End point values	MenABCWY+OMV Group	MenACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	46		
Units: Titers				
geometric mean (confidence interval 95%)				
Serogroup B, M14459; Day 1 (N=33;46)	2.04 (1.46 to 2.83)	1.37 (1.12 to 1.69)		
Serogroup B, M14459; Day 4 (N=33;23)	1.99 (1.44 to 2.75)	1.22 (0.96 to 1.54)		
Serogroup B, M14459; Day 8 (N=33;22)	17 (9.31 to 30)	1.52 (1.05 to 2.20)		
Serogroup B, M14459; Day 31 (N=33;45)	24 (14 to 42)	2.83 (1.88 to 4.24)		
Serogroup B, M01-0240364; Day 1 (N=31;44)	2.26 (1.26 to 4.08)	1.14 (0.97 to 1.35)		
Serogroup B, M01-0240364; Day 4 (N=30;23)	2.50 (1.25 to 5.02)	1.36 (1.02 to 1.82)		
Serogroup B, M01-0240364; Day 8 (N=29;21)	525 (257 to 1074)	1.65 (0.79 to 3.43)		
Serogroup B, M01-0240364; Day 31 (N=30;44)	601 (339 to 1064)	3.05 (1.77 to 5.26)		
Serogroup B, NZ98/254; Day 1 (N=33;46)	1.81 (1.30 to 2.51)	1.35 (1.15 to 1.59)		
Serogroup B, NZ98/254; Day 4 (N=33;23)	1.90 (1.41 to 2.57)	1.89 (1.38 to 2.59)		
Serogroup B, NZ98/254; Day 8 (N=33;22)	8.19 (5.45 to 12)	1.52 (1.12 to 2.06)		
Serogroup B, NZ98/254; Day 31 (N=33;46)	13 (8.50 to 18)	3.57 (2.37 to 5.38)		
Serogroup B, M10713; Day 1 (N=33;46)	3.66 (2.38 to 5.62)	2.56 (1.74 to 3.75)		
Serogroup B, M10713; Day 4 (N=32;23)	4.16 (2.70 to 6.41)	3.73 (2.10 to 6.65)		
Serogroup B, M10713; Day 8 (N=33;22)	15 (9.26 to 23)	2.03 (1.30 to 3.17)		
Serogroup B, M10713; Day 31 (N=33;46)	20 (13 to 31)	5.51 (3.45 to 8.79)		
Serogroup B, H44/76; Day 1 (N=33;46)	2.33 (1.57 to 3.45)	1.21 (1.03 to 1.42)		
Serogroup B, H44/76; Day 4 (N=33;23)	2.58 (1.78 to 3.75)	1.38 (1.05 to 1.81)		
Serogroup B, H44/76; Day 8 (N=33;22)	64 (38 to 109)	1.84 (1.18 to 2.89)		

Serogroup B, H44/76; Day 31 (N=33;46)	98 (57 to 170)	5.78 (3.59 to 9.31)		
Serogroup B, 5/99; Day 1 (N=33;46)	13 (7.29 to 22)	1.78 (1.36 to 2.34)		
Serogroup B, 5/99; Day 4 (N=33;23)	17 (9.56 to 31)	1.99 (1.36 to 2.92)		
Serogroup B, 5/99; Day 8 (N=33;22)	1768 (1204 to 2596)	1.97 (0.88 to 4.42)		
Serogroup B, 5/99; Day 31 (N=33;46)	1426 (940 to 2164)	19 (11 to 34)		
Serogroup A; Day 1 (N=33;46)	4.06 (2.22 to 7.44)	6.64 (3.56 to 12)		
Serogroup A; Day 4 (N=33;23)	3.85 (2.00 to 7.42)	9.69 (3.90 to 24)		
Serogroup A; Day 8 (N=33;22)	474 (321 to 701)	61 (25 to 146)		
Serogroup A; Day 31 (N=33;46)	396 (288 to 545)	149 (106 to 210)		
Serogroup C; Day 1 (N=32;46)	17 (7.80 to 37)	6.62 (4.10 to 11)		
Serogroup C; Day 4 (N=30;22)	21 (9.93 to 43)	12 (5.13 to 29)		
Serogroup C; Day 8 (N=29;19)	2664 (1840 to 3855)	1710 (979 to 2985)		
Serogroup C; Day 31 (N=30;38)	1676 (1164 to 2414)	1199 (849 to 1692)		
Serogroup W; Day 1 (N=32;46)	28 (15 to 53)	25 (15 to 40)		
Serogroup W; Day 4 (N=25;22)	19 (8.77 to 41)	20 (8.11 to 51)		
Serogroup W; Day 8 (N=25;16)	1285 (900 to 1833)	1693 (924 to 3103)		
Serogroup W; Day 31 (N=28;38)	1823 (1163 to 2856)	2259 (1678 to 3041)		
Serogroup Y; Day 1 (N=32;44)	6.17 (3.00 to 13)	12 (6.29 to 22)		
Serogroup Y; Day 4 (N=31;22)	6.53 (3.05 to 14)	9.60 (3.56 to 26)		
Serogroup Y; Day 8 (N=23;13)	722 (429 to 1216)	1133 (710 to 1809)		
Serogroup Y; Day 31 (N=23;23)	779 (430 to 1413)	1692 (1206 to 2373)		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean hSBA Titers (GMTs) against N. meningitidis serogroups A, C, W and Y and serogroup B test strains.

End point title	Geometric Mean hSBA Titers (GMTs) against N. meningitidis serogroups A, C, W and Y and serogroup B test strains.[21]

End point description:

GMTs at Day 1, 31, 34, 38, 61 as measure of the kinetics of the immune response following a dose of MenABCWY+OMV, in subjects who were not primed with any meningococcal vaccine (i.e., Naïve Group). This outcome measure reports data for only the Naïve Group as per protocol. The Meningococcal B Strains were M14459, M01-0240364, NZ98/254, M10713, H44/76 and 5/99.
The analysis was performed on FAS immunogenicity kinetics population set, which included all subjects in the Enrolled population who received a study vaccination, provided at least one evaluable serum sample post vaccination and whose assay results were available for at least one strain.

End point type	Secondary

End point timeframe:

At Days 1, 31, 34, 38 and 61

Notes:

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

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

End point values	Naive Group			
Subject group type	Reporting group			
Number of subjects analysed	50			
Units: Titers				
geometric mean (confidence interval 95%)				
Serogroup B, M14459; Day 1 (N=50)	1.48 (1.18 to 1.85)			
Serogroup B, M14459; Day 31 (N=50)	4.02 (2.67 to 6.06)			
Serogroup B, M14459; Day 34 (N=26)	5.06 (2.96 to 8.66)			
Serogroup B, M14459; Day 38 (N=24)	9.16 (5.35 to 16)			
Serogroup B, M14459; Day 61 (N=49)	9.78 (6.42 to 15)			
Serogroup B, M01-0240364; Day 1 (N=50)	1.23 (1.02 to 1.47)			
Serogroup B, M01-0240364; Day 31 (N=45)	3.11 (1.76 to 5.51)			
Serogroup B, M01-0240364; Day 34 (N=25)	5.13 (2.171 to 12)			
Serogroup B, M01-0240364; Day 38 (N=22)	75 (29 to 199)			
Serogroup B, M01-0240364; Day 61 (N=47)	21 (11 to 38)			
Serogroup B, NZ98/254; Day 1 (N=50)	1.45 (1.18 to 1.77)			
Serogroup B, NZ98/254; Day 31 (N=50)	5.75 (3.95 to 8.37)			
Serogroup B, NZ98/254; Day 34 (N=26)	6.93 (4.02 to 12)			
Serogroup B, NZ98/254; Day 38 (N=24)	7.92 (5.03 to 12)			
Serogroup B, NZ98/254; Day 61 (N=49)	7.50 (5.12 to 11)			
Serogroup B, M10713; Day 1 (N=50)	3.10 (2.16 to 4.45)			
Serogroup B, M10713; Day 31 (N=50)	7.70 (5.04 to 12)			
Serogroup B, M10713; Day 34 (N=23)	6.70 (3.37 to 13)			
Serogroup B, M10713; Day 38 (N=24)	8.94 (4.91 to 16)			
Serogroup B, M10713; Day 61 (N=49)	8.73 (5.80 to 13)			
Serogroup B, H44/76; Day 1 (N=50)	1.44 (1.14 to 1.80)			
Serogroup B, H44/76; Day 31 (N=50)	7.27 (4.53 to 12)			

Serogroup B, H44/76; Day 34 (N=26)	8.91 (4.62 to 17)			
Serogroup B, H44/76; Day 38 (N=24)	35 (20 to 60)			
Serogroup B, H44/76; Day 61 (N=49)	32 (21 to 49)			
Serogroup B, 5/99; Day 1 (N=50)	1.90 (1.42 to 2.53)			
Serogroup B, 5/99; Day 31 (N=50)	25 (15 to 42)			
Serogroup B, 5/99; Day 34 (N=26)	40 (18 to 90)			
Serogroup B, 5/99; Day 38 (N=24)	432 (273 to 683)			
Serogroup B, 5/99; Day 61 (N=49)	256 (194 to 338)			
Serogroup A; Day 1 (N=50)	1.20 (1.05 to 1.37)			
Serogroup A; Day 31 (N=50)	22 (14 to 35)			
Serogroup A; Day 34 (N=26)	31 (15 to 67)			
Serogroup A; Day 38 (N=24)	107 (64 to 179)			
Serogroup A; Day 61 (N=47)	74 (51 to 108)			
Serogroup C; Day 1 (N=49)	5.11 (3.49 to 7.48)			
Serogroup C; Day 31 (N=48)	58 (35 to 96)			
Serogroup C; Day 34 (N=20)	94 (54 to 162)			
Serogroup C; Day 38 (N=22)	259 (149 to 449)			
Serogroup C; Day 61 (N=47)	188 (132 to 266)			
Serogroup W; Day 1(N=47)	8.37 (4.78 to 15)			
Serogroup W; Day 31 (N=46)	117 (83 to 166)			
Serogroup W; Day 34 (N=19)	180 (107 to 305)			
Serogroup W; Day 38 (N=20)	188 (129 to 272)			
Serogroup W; Day 61 (N=41)	168 (129 to 218)			
Serogroup Y; Day 1 (N=47)	2.00 (1.40 to 2.85)			
Serogroup Y; Day 31 (N=46)	85 (45 to 163)			
Serogroup Y; Day 34 (N=23)	109 (55 to 215)			
Serogroup Y; Day 38 (N=20)	299 (180 to 495)			
Serogroup Y; Day 61 (N=43)	224 (147 to 343)			

Statistical analyses

No statistical analyses for this end point

Secondary: GMR against N. meningitidis serogroups A, C, W and Y and serogroup B test strains.

End point title	GMR against N. meningitidis serogroups A, C, W and Y and serogroup B test strains.[22]

End point description:

GMRs as measure of the kinetics of the immune response following a dose of MenABCWY+OMV, in subjects who previously received 2 doses of MenABCWY+OMV or 1 dose of MenACWY. The Meningococcal B Strains were M14459, M01-0240364, NZ98/254, M10713, H44/76 and 5/99.
The analysis was performed on FAS immunogenicity kinetics population set, which included all subjects in the Enrolled population who received a study vaccination, provided at least one evaluable serum sample post vaccination and whose assay results were available for at least one strain.

End point type	Secondary

End point timeframe:

At Days 4, 8 and 31 versus Day 1

Notes:

[22] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

End point values	MenABCWY+OMV Group	MenACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	46		
Units: Ratios				
geometric mean (confidence interval 95%)				
Serogroup B, M14459; Dy 4/Day 1 (N=33;23)	0.98 (0.88 to 1.09)	0.80 (0.60 to 1.05)		
Serogroup B, M14459; Day 8/Day 1 (N=33;22)	8.19 (4.58 to 15)	1.21 (0.80 to 1.83)		
Serogroup B, M14459; Day 31/Day 1 (N=33;45)	12 (6.88 to 20)	2.11 (1.45 to 3.07)		
Serogroup B, M01-0240364; Day 4/Day 1 (N=30;22)	1.08 (0.68 to 1.71)	1.06 (0.90 to 1.25)		
Serogroup B, M01-0240364; Day 8/Day 1 (N=28;20)	210 (85 to 517)	1.69 (0.78 to 3.66)		
Serogroup B, M01-0240364; Day 31/Day 1 (N=28;42)	229 (108 to 485)	2.80 (1.59 to 4.96)		
Serogroup B, NZ98/254; Day 4/Day 1 (N=33;23)	1.05 (0.84 to 1.31)	1.19 (0.90 to 1.58)		
Serogroup B, NZ98/254; Day 8/Day 1 (N=33;22)	4.53 (2.93 to 7.02)	1.31 (0.90 to 1.90)		
Serogroup B, NZ98/254; Day 31/Day 1 (N=33;46)	6.92 (4.61 to 10)	2.64 (1.73 to 4.02)		
Serogroup B, M10713; Day 4/Day 1 (N=32;23)	1.09 (0.93 to 1.28)	0.93 (0.76 to 1.14)		
Serogroup B, M10713; Day 8/Day 1 (N=33;22)	4.02 (2.74 to 5.88)	1.22 (0.89 to 1.67)		
Serogroup B, M10713; Day 31/Day 1 (N=33;46)	5.38 (3.54 to 8.17)	2.15 (1.46 to 3.17)		
Serogroup B, H44/76; Day 4/Day 1 (N=33;23)	1.11 (0.88 to 1.4128)	1.00 (0.79 to 1.27)		
Serogroup B, H44/76; Day 8/Day 1 (N=33;22)	28 (15 to 50)	1.73 (1.06 to 2.81)		
Serogroup B, H44/76; Day 31/Day 1 (N=33;46)	42 (25 to 72)	4.78 (2.90 to 7.89)		
Serogroup B, 5/99; Day 4/Day 1 (N=33;23)	1.35 (0.90 to 2.04)	0.93 (0.68 to 1.26)		
Serogroup B, 5/99; Day 8/Day 1 (N=33;22)	139 (77 to 248)	1.30 (0.66 to 2.57)		

Serogroup B, 5/99; Day 31/Day 1 (N=33;46)	112 (68 to 185)	11 (6.09 to 19)		
Serogroup A; Day 4/Day 1 (N=33;23)	0.95 (0.72 to 1.24)	0.87 (0.61 to 1.24)		
Serogroup A; Day 8/Day 1 (N=33;22)	117 (59 to 232)	17 (7.78 to 37)		
Serogroup A; Day 31/Day 1 (N=33;46)	98 (54 to 177)	22 (13 to 38)		
Serogroup C; Day 4/Day 1 (N=29;22)	1.30 (0.98 to 1.73)	1.20 (0.92 to 1.56)		
Serogroup C; Day 8/Day 1 (N=28;19)	164 (65 to 411)	491 (211 to 1141)		
Serogroup C; Day 31/Day 1 (N=30;38)	105 (49 to 222)	238 (145 to 392)		
Serogroup W; Day 4/Day 1 (N=25;22)	0.90 (0.56 to 1.442)	0.97 (0.68 to 1.37)		
Serogroup W; Day 8/Day 1 (N=24;16)	61 (29 to 131)	67 (27 to 168)		
Serogroup W; Day 31/Day 1 (N=28;38)	67 (34 to 132)	112 (65 to 191)		
Serogroup Y; Day 4/Day 1 (N=30;22)	1.06 (0.79 to 1.41)	0.73 (0.49 to 1.09)		
Serogroup Y; Day 8/Day 1 (N=22;13)	156 (62 to 390)	132 (33 to 535)		
Serogroup Y; Day 31/Day 1 (N=22;22)	162 (70 to 375)	216 (80 to 580)		

Statistical analyses

No statistical analyses for this end point

Secondary: GMR against N. meningitidis serogroups A, C, W and Y and serogroup B test strains.

End point title	GMR against N. meningitidis serogroups A, C, W and Y and serogroup B test strains.[23]

End point description:

GMRs as measure of the kinetics of the immune response following a dose of MenABCWY+OMV, in Naïve subjects. The Meningococcal B Strains were M14459, M01-0240364, NZ98/254, M10713, H44/76 and 5/99.
The analysis was performed on FAS immunogenicity kinetics population set, which included all subjects in the Enrolled population who received a study vaccination, provided at least one evaluable serum sample post vaccination and whose assay results were available for at least one strain.

End point type	Secondary

End point timeframe:

At Days 31, 34, 38 and 61 versus Day 1

Notes:

[23] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

End point values	Naive Group			
Subject group type	Reporting group			
Number of subjects analysed	50			
Units: Ratios				
geometric mean (confidence interval 95%)				
Serogroup B, M14459; Day 31/Day 1 (N=50)	2.72 (1.91 to 3.87)			
Serogroup B, M14459; Day 34/Day 1 (N=26)	3.45 (2.09 to 5.72)			
Serogroup B, M14459; Day 38/Day 1 (N=24)	6.15 (3.65 to 10)			
Serogroup B, M14459; Day 61/Day 1 (N=49)	6.78 (4.51 to 10)			
Serogroup B, M01-0240364; Day 31/Day 1 (N=45)	2.48 (1.51 to 4.07)			
Serogroup B, M01-0240364; Day 34/Day 1 (N=25)	3.97 (1.79 to 8.80)			
Serogroup B, M01-0240364; Day 38/Day 1 (N=22)	64 (24 to 167)			
Serogroup B, M01-0240364; Day 61/Day 1 (N=47)	18 (9.90 to 33)			
Serogroup B, NZ98/254; Day 31/Day 1 (N=50)	3.98 (2.73 to 5.79)			
Serogroup B, NZ98/254; Day 34/Day 1 (N=26)	4.52 (2.60 to 7.84)			
Serogroup B, NZ98/254; Day 38/Day 1 (N=24)	5.84 (3.34 to 10)			
Serogroup B, NZ98/254; Day 61/Day 1 (N=49)	5.28 (3.61 to 7.74)			
Serogroup B, M10713; Day 31/Day 1 (N=50)	2.48 (1.78 to 3.45)			
Serogroup B, M10713; Day 34/Day 1 (N=23)	2.54 (1.67 to 3.86)			
Serogroup B, M10713; Day 38/Day 1 (N=24)	2.83 (1.64 to 4.87)			
Serogroup B, M10713; Day 61/Day 1 (N=49)	2.85 (1.98 to 4.11)			
Serogroup B, H44/76; Day 31/Day 1 (N=50)	5.06 (3.21 to 7.97)			
Serogroup B, H44/76; Day 34/Day 1 (N=26)	6.17 (3.33 to 11)			
Serogroup B, H44/76; Day 38/Day 1 (N=24)	24 (14 to 42)			
Serogroup B, H44/76; Day 61/Day 1 (N=49)	23 (15 to 35)			
Serogroup B, 5/99; Day 31/Day 1 (N=50)	13 (8.14 to 22)			
Serogroup B, 5/99; Day 34/Day 1 (N=26)	20 (8.58 to 49)			
Serogroup B, 5/99; Day 38/Day 1 (N=24)	233 (141 to 385)			
Serogroup B, 5/99; Day 61/Day 1 (N=49)	141 (106 to 189)			
Serogroup A; Day 31/Day 1 (N=50)	18 (12 to 29)			
Serogroup A; Day 34/Day 1 (N=26)	28 (13 to 61)			
Serogroup A; Day 38/Day 1 (N=24)	82 (48 to 140)			
Serogroup A; Day 61/Day 1 (N=47)	61 (41 to 90)			
Serogroup C; Day 31/Day 1 (N=48)	12 (6.88 to 19)			
Serogroup C; Day 34/Day 1 (N=19)	18 (8.98 to 36)			

Serogroup C; Day 38/Day 1 (N=22)	64 (32 to 128)			
Serogroup C; Day 61/Day 1 (N=46)	39 (25 to 61)			
Serogroup W; Day 31/Day 1 (N=44)	16 (8.35 to 30)			
Serogroup W; Day 34/Day 1 (N=18)	42 (15 to 116)			
Serogroup W; Day 38/Day 1 (N=19)	16 (6.68 to 40)			
Serogroup W; Day 61/Day 1 (N=38)	22 (11 to 42)			
Serogroup Y; Day 31/Day 1 (N=43)	46 (23 to 92)			
Serogroup Y; Day 34/Day 1 (N=20)	69 (30 to 1601)			
Serogroup Y; Day 38/Day 1 (N=20)	134 (68 to 264)			
Serogroup Y; Day 61/Day 1 (N=40)	106 (62 to 182)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentages of Subjects with hSBA ≥ LLQ against N. meningitidis serogroups A, C, W and Y and serogroup B test strains.

End point title	Percentages of Subjects with hSBA ≥ LLQ against N. meningitidis serogroups A, C, W and Y and serogroup B test strains.

End point description:

The HT-hSBA assay format was changed in 2015 in response to CBER comments & validation of this new format & determination of the LLOQ values for the same, are ongoing. However, the old assay format was used for sample testing in this extension trial, to maintain data comparability with the parent trials. The LLOQ cut-off values for the old assay format correspond to 8 for ACWY serogroups & 5 for B strains, & this data is already available & included in the submission. The ongoing validation procedure & determination of new LLOQ values are pertinent to the new assay format for HT-hSBA & are not considered relevant to the data obtained from the testing of the V102_02E2 study. Therefore, in the Company's judgment, the results generated with pre-defined LLOQs of 8 (for ACWY) & 5 (for B strains) are final & there will be no additional data generation with new HT-hSBA LLOQ cut-offs.

End point type	Secondary

End point timeframe:

At Day 61

End point values	MenABCWY+OMV Group	MenACWY Group	Naive Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[24]	0[25]	0[26]	
Units: Percentages of subjects				
number (confidence interval 95%)	(to)	(to)	(to)	

Notes:

[24] - No additional data generation with new HT-hSBA LLOQ cut-offs

[25] - No additional data generation with new HT-hSBA LLOQ cut-offs

[26] - No additional data generation with new HT-hSBA LLOQ cut-offs.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentages of Subjects with hSBA ≥ 8 against N. meningitidis serogroups A, C, W and Y.

End point title	Percentages of Subjects with hSBA ≥ 8 against N. meningitidis serogroups A, C, W and Y.[27]

End point description:

Immunogenicity against N. meningitidis serogroup A, C, W and Y following 2 doses of MenABCWY+OMV in subjects who previously received 1 dose of MenACWY and Naïve subjects, at Day 61, as measured by percentages of subjects with hSBA ≥ 8.
The analysis was performed on FAS immunogenicity persistence population set Day 61, which included all subjects in the Enrolled population who received a study vaccination, provided at least one evaluable serum sample at 1 month post vaccination and whose assay results were available for at least one serogroup/test strain.

End point type	Secondary

End point timeframe:

At Day 61

Notes:

[27] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

End point values	MenACWY Group	Naive Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46	47		
Units: Percentages of subjects				
number (confidence interval 95%)				
Serogroup A (N=46;47)	100 (92.3 to 100.0)	94 (82.5 to 98.7)		
Serogroup C (N=34;47)	100 (89.7 to 100.0)	100 (92.5 to 100.0)		
Serogroup W (N=32;41)	100 (89.1 to 100.0)	100 (91.4 to 100.0)		
Serogroup Y (N=27;43)	100 (87.2 to 100.0)	98 (87.7 to 99.94)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentages of Subjects with hSBA ≥ 5 against N. meningitidis serogroup B test strains.

End point title	Percentages of Subjects with hSBA ≥ 5 against N. meningitidis serogroup B test strains.[28]

End point description:

Immunogenicity against N. meningitidis serogroup B test strains following 2 doses of MenABCWY+OMV in subjects who previously received 1 dose of MenACWY and Naïve subjects, at Day 61, as measured by percentages of subjects with hSBA ≥ 5. The Meningococcal B Strains were M14459, M01-0240364, NZ98/254, M10713, H44/76 and 5/99.
The analysis was performed on FAS immunogenicity persistence population set Day 61, which included all subjects in the Enrolled population who received a study vaccination, provided at least one evaluable

serum sample at 1 month post vaccination and whose assay results were available for at least one serogroup/test strain.

End point type	Secondary

End point timeframe:

At Day 61

Notes:

[28] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

End point values	MenACWY Group	Naive Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46	49		
Units: Percentages of subjects				
number (confidence interval 95%)				
Serogroup B, M14459 (N=46;49)	46 (30.9 to 61.0)	67 (52.5 to 80.1)		
Serogroup B, M01-0240364 (N=46;47)	65 (49.8 to 78.6)	70 (55.1 to 82.7)		
Serogroup B, NZ98/254 (N=46;49)	46 (30.9 to 61.0)	61 (46.2 to 74.8)		
Serogroup B, M10713 (N=46;49)	54 (39.0 to 69.1)	65 (50.4 to 78.3)		
Serogroup B, H44/76 (N=46;49)	85 (71.1 to 93.7)	88 (75.2 to 95.4)		
Serogroup B, 5/99 (N=46;49)	100 (92.3 to 100.0)	100 (92.7 to 100.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: GMTs against N. meningitidis serogroups A, C, W and Y and serogroup B test strains.

End point title	GMTs against N. meningitidis serogroups A, C, W and Y and serogroup B test strains.[29]

End point description:

GMTs as measure of the immunogenicity of 2 doses of MenABCWY+OMV in subjects who previously received 1 dose of MenACWY and Naïve subjects, at Day 61. The Meningococcal B Strains were M14459, M01-0240364, NZ98/254, M10713, H44/76 and 5/99.
The analysis was performed on FAS immunogenicity persistence population set Day 61, which included all subjects in the Enrolled population who received a study vaccination, provided at least one evaluable serum sample at 1 month post vaccination and whose assay results were available for at least one serogroup/test strain.

End point type	Secondary

End point timeframe:

At Day 61

Notes:

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

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

End point values	MenACWY Group	Naive Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46	49		
Units: Titers				
geometric mean (confidence interval 95%)				
Serogroup B, M14459 (N=46;49)	4.82 (3.26 to 7.12)	9.78 (6.42 to 15)		
Serogroup B, M01-0240364 (N=46;47)	19 (10 to 34)	21 (11 to 38)		
Serogroup B, NZ98/254 (N=46;49)	6.24 (4.47 to 8.70)	7.50 (5.12 to 11)		
Serogroup B, M10713 (N=46;49)	6.91 (4.43 to 11)	8.73 (5.80 to 13)		
Serogroup B, H44/76 (N=46;49)	19 (13 to 28)	32 (21 to 49)		
Serogroup B, 5/99 (N=46;49)	196 (149 to 257)	256 (194 to 338)		
Serogroup A (N=46;47)	222 (170 to 290)	74 (51 to 108)		
Serogroup C (N=34;47)	879 (712 to 1085)	188 (132 to 266)		
Serogroup W (N=32;41)	1440 (1078 to 1924)	168 (129 to 218)		
Serogroup Y (N=27;43)	1576 (1190 to 2087)	224 (147 to 343)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description: Between-group GMT ratios against N. meningitidis Serogroup B, M14459	
Comparison groups	MenACWY Group v Naive Group
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	0.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.28
upper limit	0.87

Statistical analysis title	Statistical analysis 2

Statistical analysis description:	
Between-group GMT ratios against N. meningitidis Serogroup B, M01-0240364	
Comparison groups	MenACWY Group v Naive Group
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	0.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.4
upper limit	2.11

Statistical analysis title	Statistical analysis 3
Statistical analysis description:	
Between-group GMT ratios against N. meningitidis serogroup B, NZ98/254	
Comparison groups	MenACWY Group v Naive Group
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	0.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5
upper limit	1.38

Statistical analysis title	Statistical analysis 4
Statistical analysis description:	
Between-group GMT ratios against N. meningitidis serogroup B, M10713	
Comparison groups	MenACWY Group v Naive Group
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	0.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.44
upper limit	1.44

Statistical analysis title	Statistical analysis 5
Statistical analysis description: Between-group GMT ratios against N. meningitidis serogroup B, H44/76	
Comparison groups	MenACWY Group v Naive Group
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.34
upper limit	1.07

Statistical analysis title	Statistical analysis 6
Statistical analysis description: Between-group GMT ratios against N. meningitidis serogroup B, 5/99	
Comparison groups	MenACWY Group v Naive Group
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	0.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.52
upper limit	1.12

Statistical analysis title	Statistical analysis 7
Statistical analysis description: Between-group GMT ratios against N. meningitidis serogroup A	
Comparison groups	MenACWY Group v Naive Group
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	2.99

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.89
upper limit	4.75

Statistical analysis title	Statistical analysis 8
Statistical analysis description:	
Between-group GMT ratios against N. meningitidis serogroup C	
Comparison groups	MenACWY Group v Naive Group
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	4.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.01
upper limit	7.31

Statistical analysis title	Statistical analysis 9
Statistical analysis description:	
Between-group GMT ratios against N. meningitidis serogroup W	
Comparison groups	MenACWY Group v Naive Group
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	8.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.84
upper limit	13

Statistical analysis title	Statistical analysis 10
Statistical analysis description:	
Between-group GMT ratios against N. meningitidis serogroup Y	
Comparison groups	MenACWY Group v Naive Group

Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen score method
Parameter estimate	Geometric mean ratio
Point estimate	7.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.96
upper limit	12

Secondary: GMRs against N. meningitidis serogroups A, C, W and Y and serogroup B test strains.

End point title	GMRs against N. meningitidis serogroups A, C, W and Y and serogroup B test strains.[30]

End point description:

GMRs as measure of the immunogenicity of 2 doses of MenABCWY+OMV in subjects who previously received 1 dose of MenACWY and Naïve subjects. The Meningococcal B Strains were M14459, M01-0240364, NZ98/254, M10713, H44/76 and 5/99.
The analysis was performed on FAS immunogenicity persistence population set Day 61, which included all subjects in the Enrolled population who received a study vaccination, provided at least one evaluable serum sample at 1 month post vaccination and whose assay results were available for at least one serogroup/test strain.

End point type	Secondary

End point timeframe:

Day 61 versus Day 1 (baseline)

Notes:

[30] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

End point values	MenACWY Group	Naive Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46	49		
Units: Ratios				
geometric mean (confidence interval 95%)				
Serogroup B, M14459 (N=46;49)	3.50 (2.33 to 5.26)	6.78 (4.51 to 10)		
Serogroup B, M01-0240364 (N=44;47)	16 (8.77 to 31)	18 (9.90 to 33)		
Serogroup B, NZ98/254 (N=46;49)	4.61 (3.22 to 6.60)	5.28 (3.61 to 7.74)		
Serogroup B, M10713 (N=46;49)	2.70 (1.94 to 3.77)	2.85 (1.98 to 4.11)		
Serogroup B, H44/76 (N=46;49)	16 (10 to 24)	23 (15 to 35)		
Serogroup B, 5/99 (N=46;49)	110 (76 to 159)	141 (106 to 189)		
Serogroup A (N=46;47)	33 (20 to 56)	61 (41 to 90)		

Serogroup C (N=34;46)	181 (108 to 303)	39 (25 to 61)		
Serogroup W (N=32;38)	85 (46 to 155)	22 (11 to 42)		
Serogroup Y (N=26;40)	264 (117 to 598)	106 (62 to 182)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any unsolicited and solicited adverse events (AEs) within 30 min after each vaccination.

End point title	Number of subjects reporting any unsolicited and solicited adverse events (AEs) within 30 min after each vaccination.

End point description:

Any solicited and unsolicited AEs reported within 30 minutes after each vaccination. Assessed solicited local symptoms were: Erythema and Induration. Any = occurrence of the symptom spreading beyond 25 millimeters (mm) of injection site. Assessed solicited general symptoms were: Arthralgia, Chills, Fatigue, Headache, Loss of Appetite, Myalgia, Nausea and Fever (body temperature ≥ 38°C). Other solicited data included: Prevention of Pain and/or Fever and Treatment of Pain and/or Fever. Any = occurrence of the symptom regardless of intensity grade. Note: There were no unsolicited AEs reported within 30 minutes after vaccination.
The analysis was performed on the Solicited safety Set, which included all subjects in the FAS Immunogenicity population who provided post vaccination safety data.

End point type	Secondary

End point timeframe:

Within 30 min after each vaccination

End point values	MenABCWY+OMV Group	MenACWY Group	Naive Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	46	50	
Units: Subjects				
Erythema (1st vaccination) (N=33;46;50)	0	1	0	
Erythema (2nd vaccination) (N=0;44;50)	0	1	0	
Induration (1st vaccination) (N=33;46;50)	0	0	0	
Induration (2nd vaccination) (N=0;44;50)	0	0	0	
Pain (1st vaccination) (N=33;46;50)	4	8	6	
Pain (2nd vaccination) (N=0;44;50)	0	3	4	
Arthralgia (1st vaccination) (N=33;46;50)	0	0	0	
Arthralgia (2nd vaccination) (N=0;44;50)	0	0	0	
Chills (1st vaccination) (N=33;46;50)	0	0	0	
Chills (2nd vaccination) (N=0;44;50)	0	0	0	
Fatigue (1st vaccination) (N=33;46;50)	0	0	0	
Fatigue (2nd vaccination) (N=0;44;50)	0	0	1	

Headache (1st vaccination) (N=33;46;50)	1	0	0	
Headache (2nd vaccination) (N=0;44;50)	0	0	1	
Loss of Appetite (1st vaccination) (N=33;46;50)	0	0	0	
Loss of Appetite (2nd vaccination) (N=0;44;50)	0	0	0	
Myalgia (1st vaccination) (N=33;46;50)	0	0	0	
Myalgia (2nd vaccination) (N=0;44;50)	0	0	0	
Nausea (1st vaccination) (N=33;46;50)	0	0	0	
Nausea (2nd vaccination) (N=0;44;50)	0	0	0	
Fever (1st vaccination) (N=33;46;50)	0	0	0	
Fever (2nd vaccination) (N=0;44;50)	0	0	0	
Prevention of Pain/Fever (1st vacc.) (N=33;45;50)	0	0	0	
Prevention of Pain/Fever (2nd vacc.) (N=0;44;50)	0	0	1	
Treatment of Pain/Fever (1st vacc.) (N=33;45;50)	0	0	0	
Treatment of Pain/Fever (2nd vacc.) (N=0;44;50)	0	0	2	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any solicited local symptoms.

End point title	Number of subjects with any solicited local symptoms.

End point description:

Assessed solicited local symptoms were Erythema, Induration and Pain. Any = occurrence of the symptom spreading beyond 25 millimeters (mm) of injection site.
The analysis was performed on the Solicited safety Set, which included all subjects in the FAS Immunogenicity population who provided post vaccination safety data.

End point type	Secondary

End point timeframe:

From Day 1 (6 hours) to Day 7 after each vaccination

End point values	MenABCWY+OMV Group	MenACWY Group	Naive Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	46	50	
Units: Subjects				
Any local AEs (1st vaccination) (N=33;46;50)	31	41	47	
Erythema (1st vaccination) (N=33;45;50)	8	7	8	
Induration (1st vaccination) (N=33;46;50)	12	7	13	
Pain (1st vaccination) (N=33;46;50)	31	41	47	

Any local AEs (2nd vaccination) (N=0;45;50)	0	35	41	
Erythema (2nd vaccination) (N=0;45;49)	0	6	7	
Induration (2nd vaccination) (N=0;45;50)	0	9	8	
Pain (2nd vaccination) (N=0;45;50)	0	34	41	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with solicited systemic symptoms and other solicited data.

End point title	Number of subjects with solicited systemic symptoms and other solicited data.

End point description:

Assessed solicited systemic symptoms were Arthralgia, Chills, Fatigue, Headache, Loss of Appetite, Myalgia, Nausea and Fever (body temperature ≥ 38°C). Other solicited data included: Prevention of pain and/or fever and Treatment of pain and/or fever. Any = occurrence of the symptom regardless of intensity grade.
The analysis was performed on the Solicited safety Set, which included all subjects in the FAS Immunogenicity population who provided post vaccination safety data.

End point type	Secondary

End point timeframe:

From Day 1 (6 hours) to Day 7 after each vaccination

End point values	MenABCWY+OMV Group	MenACWY Group	Naive Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	46	50	
Units: Subjects				
Any systemic AEs (1st vaccination) (N=33;46;50)	24	35	37	
Arthralgia (1st vaccination) (N=33;46;50)	8	8	15	
Chills (1st vaccination) (N=33;46;50)	5	11	11	
Fatigue (1st vaccination) (N=33;45;50)	14	19	24	
Headache (1st vaccination) (N=33;46;50)	19	20	23	
Loss of Appetite (1st vaccination) (N=33;45;50)	5	9	9	
Myalgia (1st vaccination) (N=33;46;50)	18	22	23	
Nausea (1st vaccination) (N=33;46;50)	4	10	13	
Fever (1st vaccination) (N=33;46;50)	0	4	8	
Prevention of Pain/Fever (1st vacc.) (N=33;44;50)	0	1	1	
Treatment of Pain/Fever (1st vacc.) (N=33;44;50)	8	7	11	
Any systemic AEs (2nd vaccination) (N=0;45;50)	0	22	28	

Arthralgia (2nd vaccination) (N=0;45;50)	0	4	7	
Chills (2nd vaccination) (N=0;45;50)	0	5	9	
Fatigue (2nd vaccination) (N=0;44;50)	0	10	12	
Headache (2nd vaccination) (N=0;44;50)	0	11	18	
Loss of Appetite (2nd vaccination) (N=0;45;50)	0	3	5	
Myalgia (2nd vaccination) (N=0;45;50)	0	12	14	
Nausea (2nd vaccination) (N=0;45;50)	0	4	4	
Fever (2nd vaccination) (N=0;45;50)	0	4	2	
Prevention of Pain/Fever (2nd vacc.) (N=0;45;50)	0	1	3	
Treatment of Pain/Fever (2nd vacc.) (N=0;45;50)	0	2	6	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with unsolicited Adverse Events (AEs).

End point title	Number of subjects with unsolicited Adverse Events (AEs).

End point description:

An unsolicited AE covers 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 and reported in addition to those solicited during the clinical study and any solicited symptom with onset outside the specified period of follow-up for solicited symptoms. Any was defined as the occurrence of any unsolicited AE regardless of intensity grade or relation to vaccination. Possibly or Probably related = AE assessed by the investigator as related to the vaccination.
The analysis was performed on the Unsolicited Safety Set, which included all subjects in the Exposed Set who had post vaccination unsolicited adverse event records.

End point type	Secondary

End point timeframe:

From Day 1 to Day 31 after each vaccination (Day 1 to Day 31 for MenABCWY+OMV Group and Day 1 to Day 61 for MenACWY and Naive Groups)

End point values	MenABCWY+OMV Group	MenACWY Group	Naive Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	46	50	
Units: Subjects				
Any AEs	11	21	20	
Possibly or Probably Related AEs	3	11	8	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with medically attended AEs reported during the entire study period.

End point title	Number of subjects with medically attended AEs reported during the entire study period.

End point description:

Medically attended AEs = were defined as events for which the subject received medical attention defined as hospitalization, an emergency room visit, or a visit to or from medical personnel (medical doctor) for any reason. Any medically attended AE(s) = Occurrence of any medically attended AE(s) regardless of intensity grade or relation to vaccination.
The analysis was performed on the Unsolicited Safety Set, which included all subjects in the Exposed Set who had post vaccination unsolicited adverse event records.

End point type	Secondary

End point timeframe:

During the entire study period (Day 1 to Day 31 for MenABCWY+OMV Group and Day 1 to Day 61 for MenACWY and Naive Groups)

End point values	MenABCWY+OMV Group	MenACWY Group	Naive Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	46	50	
Units: Subjects				
Medically attended AEs	2	6	5	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with unsolicited AEs leading to premature withdrawal from study reported during the entire study period.

End point title	Number of subjects with unsolicited AEs leading to premature withdrawal from study reported during the entire study period.

End point description:

The number of subjects who reported unsolicited AEs leading to premature withdrawal from study after any vaccination.
The analysis was performed on the Unsolicited Safety Set, which included all subjects in the Exposed Set who had post vaccination unsolicited adverse event records.

End point type	Secondary

End point timeframe:

From Day 1 to Day 31 (MenABCWY+OMV Group) and from Day 1 to Day 61 (MenACWY and Naive Groups)

End point values	MenABCWY+OMV Group	MenACWY Group	Naive Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	46	50	
Units: Subjects				
AEs leading to premature withdrawal	0	1	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with serious adverse events (SAEs) reported during the entire study period.

End point title	Number of subjects with serious adverse events (SAEs) reported during the entire study period.

End point description:

Serious adverse events (SAEs) assessed include medical occurrences that result in death, are life threatening, require hospitalization or prolongation of hospitalization or result in disability/incapacity.
Any SAE(s) = Occurrence of any SAE(s) regardless of intensity grade or relation to vaccination. Possibly or probably related SAE(s) = SAE(s) assessed by the investigator as related to the vaccination.
The analysis was performed on the Unsolicited Safety Set, which included all subjects in the Exposed Set who had post vaccination unsolicited adverse event records.

End point type	Secondary

End point timeframe:

During the entire study period (Day 1 to Day 31 for MenABCWY+OMV Group and Day 1 to Day 61 for MenACWY and Naive Groups)

End point values	MenABCWY+OMV Group	MenACWY Group	Naive Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	33	46	50	
Units: Subjects				
Any SAEs	0	0	0	
Possibly or probably related SAEs	0	0	0	
AEs leading to death	0	0	0	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited local and systemic symptoms: from Day 1 (6 hours) to Day 7 after each study vaccination; Unsolicited AEs: from Day 1 to Day 31 after each study vaccination; SAEs: during the entire study period (from Day 1 to Day 61).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	MenABCWY+OMV Group

Reporting group description:

Subjects who received 2 doses of MenABCWY+OMV vaccine in the parent study V102_02 (NCT01210885) and received no subsequent meningococcal vaccines, received a booster dose of MenABCWY+OMV vaccine in the current study at Day 1.

Reporting group title	Naive Group

Reporting group description:

Subjects similar in age to subjects in the MenABCWY+OMV and MenACWY groups, who had not previously received any meningococcal vaccine and who received 2 doses of MenABCWY+OMV vaccine, 1 month apart (Day 1 and Day 31), in the current study.

Reporting group title	MenACWY Group

Reporting group description:

Subjects who received MenACWY vaccine in the parent study V102_02 (NCT01210885) and received no subsequent meningococcal vaccines, received 2 doses of MenABCWY+OMV vaccine, one month apart (Day 1 and Day 31), in the current study.

Serious adverse events	MenABCWY+OMV Group	Naive Group	MenACWY Group
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 33 (0.00%)	0 / 50 (0.00%)	0 / 46 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

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

Non-serious adverse events	MenABCWY+OMV Group	Naive Group	MenACWY Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	33 / 33 (100.00%)	48 / 50 (96.00%)	44 / 46 (95.65%)
Nervous system disorders			
Headache			

subjects affected / exposed	19 / 33 (57.58%)	28 / 50 (56.00%)	23 / 46 (50.00%)
occurrences (all)	43	120	84
General disorders and administration site conditions			
Chills			
subjects affected / exposed	5 / 33 (15.15%)	16 / 50 (32.00%)	14 / 46 (30.43%)
occurrences (all)	10	31	25
Fatigue			
subjects affected / exposed	14 / 33 (42.42%)	27 / 50 (54.00%)	20 / 46 (43.48%)
occurrences (all)	29	82	75
Injection site erythema			
subjects affected / exposed	11 / 33 (33.33%)	30 / 50 (60.00%)	26 / 46 (56.52%)
occurrences (all)	45	123	135
Injection site induration			
subjects affected / exposed	18 / 33 (54.55%)	30 / 50 (60.00%)	27 / 46 (58.70%)
occurrences (all)	75	169	173
Injection site pain			
subjects affected / exposed	31 / 33 (93.94%)	48 / 50 (96.00%)	42 / 46 (91.30%)
occurrences (all)	114	333	295
Pyrexia			
subjects affected / exposed	0 / 33 (0.00%)	10 / 50 (20.00%)	8 / 46 (17.39%)
occurrences (all)	0	13	12
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	4 / 33 (12.12%)	15 / 50 (30.00%)	10 / 46 (21.74%)
occurrences (all)	11	25	30
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	8 / 33 (24.24%)	19 / 50 (38.00%)	11 / 46 (23.91%)
occurrences (all)	14	51	35
Myalgia			
subjects affected / exposed	18 / 33 (54.55%)	26 / 50 (52.00%)	25 / 46 (54.35%)
occurrences (all)	42	96	85
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	1 / 33 (3.03%)	1 / 50 (2.00%)	6 / 46 (13.04%)
occurrences (all)	1	1	6

Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	5 / 33 (15.15%) 11	13 / 50 (26.00%) 30	11 / 46 (23.91%) 25

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 November 2014	Allow pregnancy test be performed in urine or blood sample.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported