Clinical trial results:
A Phase 2, Observer Blinded, Controlled, Randomized Multi-Center Study in Adolescents, to Evaluate Safety, Tolerability and Immunogenicity of Four Different rMenB plus MenACWY Formulations.

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

Summary

EudraCT number	2014-005160-15
Trial protocol	Outside EU/EEA
Global end of trial date	27 July 2011

Results information

Result version number	v2 (current)
This version publication date	04 June 2016
First version publication date	06 June 2015
Version creation reason	• Correction of full data set re-QC of this study is necessary because of the EudraCT system glitch and updates to results are required.

Trial information

Trial identification

Sponsor protocol code	V102_02

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01210885
WHO universal trial number (UTN)	-

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001260-PIP01-11
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	06 March 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 July 2011
Global end of trial reached?	Yes
Global end of trial date	27 July 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the immunogenicity, safety and tolerability of two doses of four different formulations of Meningococcal B Recombinant Vaccine (rMenB) (± Outer Membrane Vesicles (OMV)) + Meningococcal ACWY Conjugate (MenACWY), when administered to healthy adolescents aged 11-18 years, in order to select the formulation to bring into clinical development.

Protection of trial subjects:

This clinical study was designed, implemented and reported in accordance with the International Conference on Harmonization (ICH) Harmonized Tripartite Guidelines for Good Clinical Practices (GCP), with applicable local regulations (including the European Directive 2001/20/EC, the US Code of Federal Regulation (CFR) Title 21, and the Japanese Ministry of Health, Labor, and Welfare), and with the ethical principles laid down in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 December 2010
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Colombia: 121
Country: Number of subjects enrolled	Chile: 48
Country: Number of subjects enrolled	Panama: 326
Worldwide total number of subjects	495
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0

Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	76
Adolescents (12-17 years)	383
Adults (18-64 years)	36
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Study centres were located in Panama (6 centres), Chile (2 centres) and Columbia (3 centres).

Pre-assignment

Screening details:

All subjects enrolled were included in the trial.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	MenABCWY

Arm description:

MenABCWY combination vaccine containing rMenB without outer membrane vesicle (OMV) at a 0, 2-month schedule.

Arm type	Experimental
Investigational medicinal product name	Combined MenABCWY vaccine (rMenB (no OMV) + MenACWY lyophilized)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Each dose of 0.5mL was administered.

Arm title	MenAB (X2)CWY

Arm description:

MenABCWY combination vaccine containing rMenBx2doses at a 0, 2-month schedule.

Arm type	Experimental
Investigational medicinal product name	Combined MenABCWY vaccine (rMenBx2doses (no OMV) + MenACWY lyophilized)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Each dose of 1.0mL was administered.

Arm title	MenABCWY+OMV

Arm description:

MenABCWY combination vaccine containing rMenB + OMV at 0, 2-month schedule.

Arm type	Experimental

Investigational medicinal product name	Combined MenABCWY vaccine (rMenB + OMV liquid suspension + MenACWY lyophilized)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and suspension for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Each dose of 0.5mL was administered.

Arm title	MenABCWY+¼OMV

Arm description:

MenABCWY combination vaccine containing rMenB + ¼ OMV at 0, 2-month schedule.

Arm type	Experimental
Investigational medicinal product name	Combined MenABCWY vaccine (rMenB + 1/4 OMV liquid suspension)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and suspension for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Each dose of 0.5mL was administered.

Arm title	MenB

Arm description:

rMenB (no OMV) at a 0, 2-month schedule.

Arm type	Active comparator
Investigational medicinal product name	Recombinant MenB (no OMV) vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Each dose of 0.5mL was administered.

Arm title	MenACWY/Placebo

Arm description:

1 dose of MenACWY, 1 dose of placebo at a 0, 2-month schedule.

Arm type	Placebo
Investigational medicinal product name	Menveo® Meningococcal (Groups A, C, Y, and W-135) Oligosaccharide Diphtheria CRM197 Conjugate Vaccine/Placebo.
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

MenACWY: Each dose of 0.5mL
Placebo: Each dose of 0.5 mL was administered.

Number of subjects in period 1	MenABCWY	MenAB (X2)CWY	MenABCWY+OMV
Started	80	82	83
Completed	79	80	81
Not completed	1	2	2
Consent withdrawn by subject	1	-	1
Adverse event, non-fatal	-	1	-
Lost to follow-up	-	1	-
Administrative reason	-	-	1
Protocol deviation	-	-	-

Number of subjects in period 1	MenABCWY+¼OMV	MenB	MenACWY/Placebo
Started	82	85	83
Completed	81	81	83
Not completed	1	4	0
Consent withdrawn by subject	-	4	-
Adverse event, non-fatal	-	-	-
Lost to follow-up	-	-	-
Administrative reason	-	-	-
Protocol deviation	1	-	-

Baseline characteristics

Reporting groups	
Reporting group title	MenABCWY
Reporting group description:	
MenABCWY combination vaccine containing rMenB without outer membrane vesicle (OMV) at a 0, 2-month schedule.	
Reporting group title	MenAB (X2)CWY
Reporting group description:	
MenABCWY combination vaccine containing rMenBx2doses at a 0, 2-month schedule.	
Reporting group title	MenABCWY+OMV
Reporting group description:	
MenABCWY combination vaccine containing rMenB + OMV at 0, 2-month schedule.	
Reporting group title	MenABCWY+¼OMV
Reporting group description:	
MenABCWY combination vaccine containing rMenB + ¼ OMV at 0, 2-month schedule.	
Reporting group title	MenB
Reporting group description:	
rMenB (no OMV) at a 0, 2-month schedule.	
Reporting group title	MenACWY/Placebo
Reporting group description:	
1 dose of MenACWY, 1 dose of placebo at a 0, 2-month schedule.	

Reporting group values	MenABCWY	MenAB (X2)CWY	MenABCWY+OMV
Number of subjects	80	82	83
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	13.6	13.8	13.8
standard deviation	± 2.1	± 2.1	± 2.3
Gender categorical Units: Subjects			
Female	47	44	44
Male	33	38	39

Reporting group values	MenABCWY+¼OMV	MenB	MenACWY/Placebo
Number of subjects	82	85	83
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	13.9	14.4	14.2
standard deviation	± 1.9	± 2.2	± 2.2
Gender categorical Units: Subjects			
Female	38	44	45

Male	44	41	38

Reporting group values	Total		
Number of subjects	495		
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	- -		
Gender categorical Units: Subjects			
Female	262		
Male	233		

End points

End points reporting groups

Reporting group title	MenABCWY
Reporting group description:	
MenABCWY combination vaccine containing rMenB without outer membrane vesicle (OMV) at a 0, 2-month schedule.	
Reporting group title	MenAB (X2)CWY
Reporting group description:	
MenABCWY combination vaccine containing rMenBx2doses at a 0, 2-month schedule.	
Reporting group title	MenABCWY+OMV
Reporting group description:	
MenABCWY combination vaccine containing rMenB + OMV at 0, 2-month schedule.	
Reporting group title	MenABCWY+¼OMV
Reporting group description:	
MenABCWY combination vaccine containing rMenB + ¼ OMV at 0, 2-month schedule.	
Reporting group title	MenB
Reporting group description:	
rMenB (no OMV) at a 0, 2-month schedule.	
Reporting group title	MenACWY/Placebo
Reporting group description:	
1 dose of MenACWY, 1 dose of placebo at a 0, 2-month schedule.	
Subject analysis set title	All enrolled population
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
all subjects who had signed an informed consent, undergone screening procedure (s) and were randomized.	
Subject analysis set title	Safety population
Subject analysis set type	Safety analysis
Subject analysis set description:	
all subjects in the Exposed population who: - had received at least one dose of study vaccine, - provided some post-vaccination safety data.	
Subject analysis set title	Modified Intention-to-treat (MITT) population, Immunogenicity
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
all subjects in the enrolled population who: - actually received a study vaccination; - provided at least one evaluable serum sample at the relevant time points and whose assay result was available for at least one serogroup or strain.	
Subject analysis set title	Per protocol (PP) population, Immunogenicity
Subject analysis set type	Per protocol
Subject analysis set description:	
all subjects in the MITT Immunogenicity population who: - correctly received the vaccine, - provided evaluable serum samples at the relevant time points, - had no major protocol violation as defined prior to unblinding.	

Primary: 1. Percentage of Subjects with Seroresponse to Neisseria Meningitidis Serogroups A, C, W and Y.

End point title	1. Percentage of Subjects with Seroresponse to Neisseria Meningitidis Serogroups A, C, W and Y.[1]
End point description:	
Percentages of Subjects with a Seroresponse against N. Meningitidis serogroups A, C, W and Y. The data	

were reported based on the Per Protocol Set (PPS).

End point type	Primary

End point timeframe:

1 month after the second vaccination (Day 91).

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: No statistical analysis is associated to this end point. Analyses were run descriptively.

End point values	MenABCWY	MenAB (X2)CWY	MenABCWY+OMV	MenABCWY+¼OMV
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	77	80	80	81
Units: Percentages of Subjects				
number (confidence interval 95%)				
MenA (Day 91; N=77,79,80,79,77,81)	97 (91 to 100)	97 (91 to 100)	98 (91 to 100)	97 (91 to 100)
MenC (Day 91; N=77,78,79,77,77,79)	95 (87 to 99)	96 (89 to 99)	95 (88 to 99)	97 (91 to 100)
MenW (Day 91; N=77,76,80,77,76,81)	74 (63 to 83)	82 (71 to 90)	76 (65 to 85)	86 (76 to 93)
MenY (Day 91; N=77,78,80,81,78,82)	95 (87 to 99)	92 (84 to 97)	96 (89 to 99)	93 (85 to 97)

End point values	MenB	MenACWY/Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	78	82		
Units: Percentages of Subjects				
number (confidence interval 95%)				
MenA (Day 91; N=77,79,80,79,77,81)	87 (77 to 94)	69 (58 to 79)		
MenC (Day 91; N=77,78,79,77,77,79)	29 (19 to 40)	65 (53 to 75)		
MenW (Day 91; N=77,76,80,77,76,81)	47 (36 to 59)	52 (40 to 63)		
MenY (Day 91; N=77,78,80,81,78,82)	4 (1 to 11)	73 (62 to 82)		

Statistical analyses

No statistical analyses for this end point

Primary: 2. Percentage of subjects with hSBA ≥ 1:8 to N. Meningitidis Serogroups A, C, W and Y.

End point title	2. Percentage of subjects with hSBA ≥ 1:8 to N. Meningitidis Serogroups A, C, W and Y.[2]

End point description:

Percentages of subjects with human serum bactericidal assay (hSBA) ≥ 1:8 to N. Meningitidis Serogroups A, C, W and Y after receiving 2 doses of MenABCWY vaccine. The data were reported based on the PPS.

End point type	Primary

End point timeframe:

1 month after the second vaccination (Day 91).

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis is associated to this end point. Analyses were run descriptively.

End point values	MenABCWY	MenAB (X2)CWY	MenABCWY+OMV	MenABCWY+¼ OMV
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	80[3]	80	80	81
Units: Percentages of Subjects				
number (confidence interval 95%)				
MenA (Day 1; N=80,80,82,81,82,82)	9 (4 to 17)	5 (1 to 12)	4 (1 to 10)	1 (0.031 to 7)
MenA (Day 91; N=77,79,80,80,77,81)	99 (93 to 100)	100 (95 to 100)	98 (91 to 100)	99 (93 to 100)
MenC (Day 1; N=80,80,82,80,82,81)	33 (22 to 44)	29 (19 to 40)	38 (27 to 49)	33 (22 to 44)
MenC (Day 91; N=77,78,79,79,77,80)	100 (95 to 100)	100 (95 to 100)	100 (95 to 100)	100 (95 to 100)
MenW (Day 1; N=80,79,82,80,81,82)	70 (59 to 80)	65 (53 to 75)	68 (57 to 78)	70 (59 to 80)
MenW (Day 91; N=77,77,80,79,77,81)	100 (95 to 100)	100 (95 to 100)	100 (95 to 100)	100 (95 to 100)
MenY (Day 1; N=80,79,82,82,82,82)	26 (17 to 37)	25 (16 to 36)	28 (19 to 39)	28 (19 to 39)
MenY (Day 91; N=77,79,80,81,78,82)	100 (95 to 100)	100 (95 to 100)	100 (95 to 100)	100 (96 to 100)

Notes:

[3] - On day 1 PPs included 80 subjects. On day 91, PPs included 77 subjects.

End point values	MenB	MenACWY/Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	78	82		
Units: Percentages of Subjects				
number (confidence interval 95%)				
MenA (Day 1; N=80,80,82,81,82,82)	1 (0.031 to 7)	5 (1 to 12)		
MenA (Day 91; N=77,79,80,80,77,81)	87 (77 to 94)	72 (60 to 81)		
MenC (Day 1; N=80,80,82,80,82,81)	29 (20 to 40)	32 (22 to 43)		
MenC (Day 91; N=77,78,79,79,77,80)	71 (60 to 81)	86 (77 to 93)		
MenW (Day 1; N=80,79,82,80,81,82)	74 (63 to 83)	68 (57 to 78)		
MenW (Day 91; N=77,77,80,79,77,81)	99 (93 to 100)	98 (91 to 100)		
MenY (Day 1; N=80,79,82,82,82,82)	26 (17 to 36)	40 (30 to 52)		
MenY (Day 91; N=77,79,80,81,78,82)	28 (19 to 40)	100 (96 to 100)		

Statistical analyses

No statistical analyses for this end point

Primary: 3. Percentage of subjects with hSBA Titers ≥ 1:4 to N. Meningitidis Serogroups A, C, W and Y.

End point title	3. Percentage of subjects with hSBA Titers ≥ 1:4 to N. Meningitidis Serogroups A, C, W and Y.[4]

End point description:

Percentages of subjects with hSBA≥1:4 against N. Meningitidis serogroups A, C, W and Y after receiving

2 doses of MenABCWY vaccine. The data were reported based on the PPS.

End point type	Primary

End point timeframe:

1 month after the second vaccination (Day 91).

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis is associated to this end point. Analyses were run descriptively.

End point values	MenABCWY	MenAB (X2)CWY	MenABCWY+OMV	MenABCWY+¼ OMV
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	80[5]	80	80	81
Units: Percentages of Subjects				
number (confidence interval 95%)				
MenA (Day 1; N=80,80,82,81,82,82)	9 (4 to 17)	8 (3 to 16)	6 (2 to 14)	1 (0.031 to 7)
MenA (Day 91; N=77,79,80,80,77,81)	99 (93 to 100)	100 (95 to 100)	99 (93 to 100)	99 (93 to 100)
MenC (Day 1; N=80,80,82,80,82,81)	45 (34 to 57)	41 (30 to 53)	50 (39 to 61)	53 (41 to 64)
MenC (Day 91; N=77,78,79,79,77,80)	100 (95 to 100)	100 (95 to 100)	100 (95 to 100)	100 (95 to 100)
MenW (Day 1; N=80,79,82,80,81,82)	71 (60 to 81)	67 (56 to 77)	70 (58 to 79)	75 (64 to 84)
MenW (Day 91; N=77,77,80,79,77,81)	100 (95 to 100)	100 (95 to 100)	100 (95 to 100)	100 (95 to 100)
MenY (Day 1; N=80,79,82,82,82,82)	33 (22 to 44)	29 (19 to 40)	32 (22 to 43)	33 (23 to 44)
MenY (Day 91; N=77,79,80,81,78,82)	100 (95 to 100)	100 (95 to 100)	100 (95 to 100)	100 (96 to 100)

Notes:

[5] - On day 1 PPs included 80 subjects. On day 91, PPs included 77 subjects.

End point values	MenB	MenACWY/Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	78	82		
Units: Percentages of Subjects				
number (confidence interval 95%)				
MenA (Day 1; N=80,80,82,81,82,82)	5 (1 to 12)	6 (2 to 14)		
MenA (Day 91; N=77,79,80,80,77,81)	88 (79 to 95)	72 (60 to 81)		
MenC (Day 1; N=80,80,82,80,82,81)	46 (35 to 58)	48 (37 to 60)		
MenC (Day 91; N=77,78,79,79,77,80)	84 (74 to 92)	95 (88 to 99)		
MenW (Day 1; N=80,79,82,80,81,82)	75 (64 to 84)	72 (61 to 81)		
MenW (Day 91; N=77,77,80,79,77,81)	99 (93 to 100)	99 (93 to 100)		
MenY (Day 1; N=80,79,82,82,82,82)	32 (22 to 43)	44 (33 to 55)		
MenY (Day 91; N=77,79,80,81,78,82)	33 (23 to 45)	100 (96 to 100)		

Statistical analyses

No statistical analyses for this end point

Primary: 4. Percentage of Subjects with Fourfold Increase in hSBA Titers for MenB

strains.

End point title	4. Percentage of Subjects with Fourfold Increase in hSBA Titers for MenB strains.[6]

End point description:

Percentages of Subjects with Fourfold Increase in hSBA Titers for the three major meningococcal B Strains (Strain 44/76-SL, Strain 5/99 and Strain NZ98/254). The data were reported based on the PPS.

End point type	Primary

End point timeframe:

1 month after the second vaccination (Day 91).

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: No statistical analysis is associated to this end point. Analyses were run descriptively.

End point values	MenABCWY	MenAB (X2)CWY	MenABCWY+OMV	MenABCWY+¼OMV
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	77	80	80	81
Units: Percentages of Subjects				
number (confidence interval 95%)				
S.44/76-SL (Day 91; N=77,78,77,79,78,81)	95 (87 to 99)	96 (89 to 99)	99 (93 to 100)	97 (91 to 100)
S.5/99 (Day 91; N=76,79,80,77,77,80)	95 (87 to 99)	100 (95 to 100)	99 (93 to 100)	100 (95 to 100)
S.NZ98/254 (Day 91; N=77,79,80,78,77,81)	10 (5 to 19)	14 (7 to 24)	46 (35 to 58)	46 (35 to 58)

End point values	MenB	MenACWY/Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	78	82		
Units: Percentages of Subjects				
number (confidence interval 95%)				
S.44/76-SL (Day 91; N=77,78,77,79,78,81)	87 (78 to 94)	1 (0.031 to 7)		
S.5/99 (Day 91; N=76,79,80,77,77,80)	99 (93 to 100)	3 (0 to 9)		
S.NZ98/254 (Day 91; N=77,79,80,78,77,81)	5 (1 to 13)	1 (0.031 to 7)		

Statistical analyses

No statistical analyses for this end point

Primary: 5. Percentage of Subjects with hSBA ≥ 1:5 for MenB strains.

End point title	5. Percentage of Subjects with hSBA ≥ 1:5 for MenB strains.[7]

End point description:

Percentages of Subjects with hSBA ≥ 1:5 to N. Meningitidis for the three major meningococcal B Strains (Strain 44/76-SL, Strain 5/99 and Strain NZ98/254). The data were reported based on the PPS.

End point type	Primary

End point timeframe:

1 month after the second vacciantion (Day 91).

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: No statistical analysis is associated to this end point. Analyses were run descriptively.

End point values	MenABCWY	MenAB (X2)CWY	MenABCWY+OMV	MenABCWY+¼ OMV
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	80[8]	80	80	81
Units: Percentages of Subjects				
number (confidence interval 95%)				
S.44/76-SL (Day 1; N=80,79,81,81,82,82)	4 (1 to 11)	8 (3 to 16)	7 (3 to 15)	6 (2 to 14)
S.44/76-SL (Day 91; N=77,79,78,80,78,81)	96 (89 to 99)	99 (93 to 100)	100 (95 to 100)	99 (93 to 100)
S.5/99 (Day 1; N=80,80,82,81,82,82)	14 (7 to 23)	13 (6 to 22)	10 (4 to 18)	14 (7 to 23)
S.5/99 (Day 91; N=76,79,80,78,77,80)	99 (93 to 100)	100 (95 to 100)	100 (95 to 100)	100 (95 to 100)
S.NZ98/254 (Day 1; N=80,80,82,81,82,82)	3 (0 to 9)	6 (2 to 14)	5 (1 to 12)	2 (0 to 9)
S.NZ98/254 (Day 91; N=77,79,80,79,77,81)	16 (8 to 26)	19 (11 to 29)	78 (67 to 86)	71 (60 to 81)

Notes:

[8] - On day 1 PPs included 80 subjects. On day 91, PPs included 77 subjects.

End point values	MenB	MenACWY/Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	78	82		
Units: Percentages of Subjects				
number (confidence interval 95%)				
S.44/76-SL (Day 1; N=80,79,81,81,82,82)	6 (2 to 14)	7 (3 to 15)		
S.44/76-SL (Day 91; N=77,79,78,80,78,81)	94 (86 to 98)	7 (3 to 15)		
S.5/99 (Day 1; N=80,80,82,81,82,82)	21 (13 to 31)	13 (7 to 23)		
S.5/99 (Day 91; N=76,79,80,78,77,80)	100 (95 to 100)	16 (9 to 26)		
S.NZ98/254 (Day 1; N=80,80,82,81,82,82)	9 (4 to 17)	4 (1 to 10)		
S.NZ98/254 (Day 91; N=77,79,80,79,77,81)	18 (10 to 29)	2 (0 to 9)		

Statistical analyses

No statistical analyses for this end point

Primary: 6. Percentage of Subjects with hSBA ≥ 1:8 for MenB strains.

End point title	6. Percentage of Subjects with hSBA ≥ 1:8 for MenB strains.[9]

End point description:

Percentages of Subjects with hSBA ≥1:8 to N. Meningitidis for the three major meningococcal B Strains

(Strain 44/76-SL, Strain 5/99 and Strain NZ98/254). The data were reported based on the PPS.

End point type	Primary

End point timeframe:

1 month after the second vaccination (Day 91).

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis is associated to this end point. Analyses were run descriptively.

End point values	MenABCWY	MenAB (X2)CWY	MenABCWY+OMV	MenABCWY+¼OMV
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	80[10]	80	80	81
Units: Percentages of Subjects				
number (confidence interval 95%)				
S.44/76-SL (Day 1; N=80,79,81,81,82,82)	3 (0 to 9)	6 (2 to 14)	6 (2 to 14)	4 (1 to 10)
S.44/76-SL (Day 91; N=77,79,78,80,78,81)	96 (89 to 99)	99 (93 to 100)	100 (95 to 100)	99 (93 to 100)
S.5/99 (Day 1; N=80,80,82,81,82,82)	10 (4 to 19)	8 (3 to 16)	5 (1 to 12)	4 (1 to 10)
S.5/99 (Day 91; N=76,79,80,78,77,80)	99 (93 to 100)	100 (95 to 100)	100 (95 to 100)	100 (95 to 100)
S.NZ98/254 (Day 1; N=80,80,82,81,82,82)	3 (0 to 9)	5 (1 to 12)	5 (1 to 12)	2 (0 to 9)
S.NZ98/254 (Day 91; N=77,79,80,79,77,81)	13 (6 to 23)	15 (8 to 25)	55 (43 to 66)	53 (42 to 64)

Notes:

[10] - On day 1 PPs included 80 subjects. On day 91, PPs included 77 subjects.

End point values	MenB	MenACWY/Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	78	82		
Units: Percentages of Subjects				
number (confidence interval 95%)				
S.44/76-SL (Day 1; N=80,79,81,81,82,82)	4 (1 to 10)	6 (2 to 14)		
S.44/76-SL (Day 91; N=77,79,78,80,78,81)	91 (82 to 96)	5 (1 to 12)		
S.5/99 (Day 1; N=80,80,82,81,82,82)	13 (7 to 23)	11 (5 to 20)		
S.5/99 (Day 91; N=76,79,80,78,77,80)	100 (95 to 100)	11 (5 to 20)		
S.NZ98/254 (Day 1; N=80,80,82,81,82,82)	6 (2 to 14)	2 (0 to 9)		
S.NZ98/254 (Day 91; N=77,79,80,79,77,81)	17 (9 to 27)	1 (0.031 to 7)		

Statistical analyses

No statistical analyses for this end point

Primary: 7. Geometric Mean hSBA Titers (GMTs), Serogroups A, C, W, Y.

End point title	7. Geometric Mean hSBA Titers (GMTs), Serogroups A, C, W, Y.

	[11]

End point description:

Geometric Mean hSBA Titers (95% CI) for N. Meningitidis Serogroups A, C, W, and Y. The data were reported based on the PPS.

End point type	Primary

End point timeframe:

1 month after the second vaccination (Day 91).

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: No statistical analysis is associated to this end point. Analyses were run descriptively.

End point values	MenABCWY	MenAB (X2)CWY	MenABCWY+OMV	MenABCWY+¼OMV
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	80[12]	80	82	81
Units: Titers				
geometric mean (confidence interval 95%)				
MenA (Day 1; N=80,80,82,80,82,81)	1.45 (1.21 to 1.72)	1.34 (1.13 to 1.6)	1.28 (1.08 to 1.52)	1.22 (1.02 to 1.45)
MenA (Day 91; N=77,79,80,80,77,81)	146 (105 to 203)	205 (148 to 283)	172 (125 to 238)	157 (114 to 218)
MenC (Day 1; N=80,79,82,80,81,82)	4.6 (3.47 to 6.11)	3.8 (2.87 to 5.03)	4.57 (3.46 to 6.04)	4.56 (3.44 to 6.05)
MenC (Day 91; N=77,78,79,79,77,80)	317 (250 to 401)	380 (301 to 481)	286 (226 to 361)	340 (268 to 431)
MenW (Day 1; N=80,79,82,82,82,82)	19 (13 to 29)	17 (11 to 26)	20 (13 to 30)	18 (12 to 28)
MenW (Day 91; N=77,77,80,79,77,81)	344 (285 to 414)	440 (365 to 531)	356 (296 to 427)	385 (320 to 464)
MenY (Day 1; N=77,77,80,79,77,81)	4.3 (3.38 to 5.47)	4.11 (3.23 to 5.23)	4.35 (3.43 to 5.52)	4.24 (3.35 to 5.39)
MenY (Day 91; N=77,79,80,81,78,82)	196 (159 to 243)	219 (178 to 271)	187 (152 to 231)	180 (147 to 221)

Notes:

[12] - On day 1 PPs included 80 subjects. On day 91, PPs included 77 subjects.

End point values	MenB	MenACWY/Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	82	82		
Units: Titers				
geometric mean (confidence interval 95%)				
MenA (Day 1; N=80,80,82,80,82,81)	1.2 (1.01 to 1.43)	1.4 (1.18 to 1.67)		
MenA (Day 91; N=77,79,80,80,77,81)	60 (43 to 84)	33 (24 to 46)		
MenC (Day 1; N=80,79,82,80,81,82)	4.59 (3.47 to 6.06)	4.04 (3.05 to 5.35)		
MenC (Day 91; N=77,78,79,79,77,80)	15 (12 to 19)	39 (31 to 49)		
MenW (Day 1; N=80,79,82,82,82,82)	22 (14 to 33)	19 (13 to 29)		
MenW (Day 91; N=77,77,80,79,77,81)	131 (108 to 158)	146 (122 to 176)		
MenY (Day 1; N=77,77,80,79,77,81)	4.45 (3.51 to 5.65)	5.76 (4.54 to 7.31)		
MenY (Day 91; N=77,79,80,81,78,82)	4.26 (3.45 to 5.25)	62 (51 to 77)		

Statistical analyses

No statistical analyses for this end point

Primary: 8. hSBA GMTs, Serogroups B strains.

End point title	8. hSBA GMTs, Serogroups B strains.[13]

End point description:

Geometric Mean hSBA Titers (95% CI) for the three major meningococcal B Strains (Strain 44/76-SL, Strain 5/99 and Strain NZ98/254). The data were reported based on the PPS.

End point type	Primary

End point timeframe:

1 month after the second vaccination (Day 91).

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: No statistical analysis is associated to this end point. Analyses were run descriptively.

End point values	MenABCWY	MenAB (X2)CWY	MenABCWY+OMV	MenABCWY+¼OMV
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	80[14]	80	80	81
Units: Titers				
geometric mean (confidence interval 95%)				
S.44/76-SL (Day 1; N=80,79,81,81,82,82)	1.17 (0.96 to 1.42)	1.33 (1.09 to 1.61)	1.34 (1.11 to 1.62)	1.24 (1.03 to 1.51)
S.44/76-SL (Day 91; N=77,79,78,80,78,81)	61 (49 to 77)	97 (78 to 123)	107 (85 to 135)	111 (88 to 139)
S.5/99 (Day 1; N=80,80,82,81,82,82)	2.38 (1.9 to 2.99)	2.09 (1.67 to 2.62)	1.83 (1.46 to 2.29)	2.01 (1.6 to 2.52)
S.5/99 (Day 91; N=76,79,80,78,77,80)	262 (217 to 317)	368 (306 to 442)	323 (269 to 389)	340 (282 to 410)
S.NZ98/254 (Day 1; N=80,80,82,81,82,82)	1.66 (1.4 to 1.96)	1.52 (1.29 to 1.79)	1.7 (1.44 to 2)	1.66 (1.4 to 1.96)
S.NZ98/254 (Day 91; N=77,79,80,79,77,81)	2.5 (1.99 to 3.14)	2.99 (2.39 to 3.74)	12 (9.98 to 16)	8.87 (7.08 to 11)

Notes:

[14] - On day 1 PPs included 80 subjects. On day 91, PPs included 77 subjects.

End point values	MenB	MenACWY/Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	78	82		
Units: Titers				
geometric mean (confidence interval 95%)				
S.44/76-SL (Day 1; N=80,79,81,81,82,82)	1.31 (1.08 to 1.59)	1.34 (1.1 to 1.62)		

S.44/76-SL (Day 91; N=77,79,78,80,78,81)	50 (40 to 63)	1.35 (1.08 to 1.7)		
S.5/99 (Day 1; N=80,80,82,81,82,82)	2.59 (2.07 to 3.24)	2.26 (1.8 to 2.82)		
S.5/99 (Day 91; N=76,79,80,78,77,80)	347 (288 to 419)	2.15 (1.78 to 2.58)		
S.NZ98/254 (Day 1; N=80,80,82,81,82,82)	1.94 (1.65 to 2.29)	1.49 (1.27 to 1.76)		
S.NZ98/254 (Day 91; N=77,79,80,79,77,81)	2.32 (1.84 to 2.91)	1.7 (1.36 to 2.13)		

Statistical analyses

No statistical analyses for this end point

Primary: 9. Geometric Mean Ratios (GMRs) for Serogroups A, C, W,Y.

End point title	9. Geometric Mean Ratios (GMRs) for Serogroups A, C, W,Y.[15]

End point description:

Geometric Mean Ratios for N. Meningitidis Serogroups A, C, W, and Y. The data were reported based on the PPS.

End point type	Primary

End point timeframe:

1 month after the second vaccination to pre-vaccination.

Notes:

[15] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis is associated to this end point. Analyses were run descriptively.

End point values	MenABCWY	MenAB (X2)CWY	MenABCWY+OMV	MenABCWY+¼ OMV
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	77	80	80	81
Units: Ratio				
geometric mean (confidence interval 95%)				
MenA (Day 91/day 1; N=77,79,80,79,77,81)	104 (73 to 147)	154 (109 to 217)	133 (95 to 187)	125 (89 to 177)
MenC (Day 91/day 1; N=77,78,79,77,77,79)	70 (50 to 99)	100 (72 to 141)	65 (46 to 91)	74 (52 to 104)
MenW (Day 91/day 1; N=77,76,80,77,76,81)	18 (12 to 28)	27 (17 to 42)	18 (12 to 28)	20 (13 to 32)
MenY (Day 91/day 1; N=77,78,80,81,78,82)	45 (34 to 60)	52 (40 to 69)	43 (32 to 56)	43 (33 to 57)

End point values	MenB	MenACWY/Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	78	82		
Units: Ratio				
geometric mean (confidence interval 95%)				

MenA (Day 91/day 1; N=77,79,80,79,77,81)	49 (35 to 70)	24 (17 to 34)		
MenC (Day 91/day 1; N=77,78,79,77,77,79)	3.32 (2.36 to 4.67)	9.61 (6.86 to 13)		
MenW (Day 91/day 1; N=77,76,80,77,76,81)	5.97 (3.81 to 9.33)	7.78 (5.04 to 12)		
MenY (Day 91/day 1; N=77,78,80,81,78,82)	0.94 (0.71 to 1.25)	12 (8.84 to 15)		

Statistical analyses

No statistical analyses for this end point

Primary: 10. GMRs for Serogroups B strains.

End point title	10. GMRs for Serogroups B strains.[16]

End point description:

Geometric Mean Ratios for the three major meningococcal B Strains (Strain 44/76-SL, Strain 5/99 and Strain NZ98/254). The data were reported based on the PPS.

End point type	Primary

End point timeframe:

1 month after 2nd vaccination to pre-vaccination.

Notes:

[16] - 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: No statistical analysis is associated to this end point. Analyses were run descriptively.

End point values	MenABCWY	MenAB (X2)CWY	MenABCWY+OMV	MenABCWY+¼ OMV
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	77	80	80	82
Units: Ratio				
geometric mean (confidence interval 95%)				
S.44/76-SL (Day 91/day 1; N=77,78,77,79,78,81)	51 (39 to 66)	74 (57 to 96)	81 (62 to 105)	88 (68 to 114)
S.5/99 (Day 91/day 1; N=76,79,80,77,77,80)	111 (85 to 145)	174 (134 to 226)	172 (133 to 223)	165 (127 to 215)
S.NZ98/254 (Day 91/day 1; N=77,79,80,78,77,81)	1.5 (1.18 to 1.9)	1.86 (1.47 to 2.36)	7.41 (5.85 to 9.37)	5.3 (4.18 to 6.72)

End point values	MenB	MenACWY/Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	78	82		
Units: Ratio				
geometric mean (confidence interval 95%)				
S.44/76-SL (Day 91/day 1; N=77,78,77,79,78,81)	38 (30 to 50)	1.08 (0.84 to 1.4)		
S.5/99 (Day 91/day 1; N=76,79,80,77,77,80)	141 (108 to 183)	1.01 (0.78 to 1.31)		

S.NZ98/254 (Day 91/day 1; N=77,79,80,78,77,81)	1.31 (1.03 to 1.66)	1.07 (0.85 to 1.35)		

Statistical analyses

No statistical analyses for this end point

Secondary: 11. Number of subjects reporting solicited local reaction during 7 days following each vaccination.

End point title	11. Number of subjects reporting solicited local reaction during 7 days following each vaccination.

End point description:

Safety was assessed as the number of subjects who reported solicited reaction from day 1 through day 7 after each vaccination (injection 1 and injection 2). The data were reported based on the Safety Set.

End point type	Secondary

End point timeframe:

Day 1 through day 7 after each vaccination on day 1 and day 61.

End point values	MenABCWY	MenAB (X2)CWY	MenABCWY+OMV	MenABCWY+¼OMV
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	80[17]	81	83	82
Units: Number of Subjects				
Pain (injection 1; N=81,81,83,82,85,82)	65	67	76	73
Pain (injection 2; N=80,80,81,81,81,82)	54	50	67	61
Erythema (injection 1; N=81,80,83,82,85,81)	19	26	31	26
Erythema (injection 2; N=80,80,81,81,81,82)	23	21	30	22
Induration (injection 1; N=81,79,83,82,84,81)	28	27	39	28
Induration (injection 2; N=80,80,81,81,81,82)	18	19	32	27
Swelling (injection 1; N=81,79,83,82,84,81)	10	22	43	20
Swelling (injection 2; N=80,80,81,81,80,82)	13	21	27	22

Notes:

[17] - 81 actually treated as per Safety Set. Difference due to "as treated" vs "as randomized" situation.

End point values	MenB	MenACWY/Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	85	82		
Units: Number of Subjects				
Pain (injection 1; N=81,81,83,82,85,82)	66	41		
Pain (injection 2; N=80,80,81,81,81,82)	56	58		

Erythema (injection 1; N=81,80,83,82,85,81)	23	20		
Erythema (injection 2; N=80,80,81,81,81,82)	19	19		
Induration (injection 1; N=81,79,83,82,84,81)	17	17		
Induration (injection 2; N=80,80,81,81,81,82)	20	18		
Swelling (injection 1; N=81,79,83,82,84,81)	16	12		
Swelling (injection 2; N=80,80,81,81,80,82)	12	15		

Statistical analyses

No statistical analyses for this end point

Secondary: 12. Number of subjects reporting solicited Systemic reaction during 7 days following each vaccination.

End point title	12. Number of subjects reporting solicited Systemic reaction during 7 days following each vaccination.

End point description:

Safety was assessed as the number of subjects who reported solicited reaction from day 1 through day 7 after each vaccination (injection 1 and injection 2). The data were reported based on the Safety Set.

End point type	Secondary

End point timeframe:

Day 1 through day 7 after each vaccination.

End point values	MenABCWY	MenAB (X2)CWY	MenABCWY+OMV	MenABCWY+¼OMV
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	80[18]	82	83	82
Units: Number of Subjects				
Chills (injection 1; N=81,81,83,82,85,82)	12	13	13	22
Chills (injection 2; N=80,80,81,81,81,82)	10	14	14	10
Malaise (injection 1; N=81,81,83,82,85,82)	19	18	14	20
Malaise (injection 2; N=80,80,81,81,81,82)	10	19	17	14
Myalgia (injection 1; N=81,81,83,82,85,82)	39	42	42	45
Myalgia (injection 2; N=80,80,81,81,81,82)	27	29	41	30
Arthralgia (injection 1; N=81,81,83,82,85,82)	17	14	14	16
Arthralgia (injection 2; N=80,80,81,81,81,82)	9	8	20	12
Headache (injection 1; N=81,81,83,82,85,82)	34	33	41	31
Headache (injection 2 N=80,80,81,81,81,82)	21	24	31	22

Fatigue (injection 1; N=81,81,83,82,85,82)	18	12	9	15
Fatigue (injection 2; N=80,80,81,81,81,82)	9	7	11	9
Nausea (injection 1; N=81,81,83,82,85,82)	15	12	13	13
Nausea (injection 2; N=80,80,81,81,81,82)	6	10	7	7
Rash (injection 1; N=81,81,83,82,85,82)	4	1	3	4
Rash (injection 2; N=80,80,81,81,81,82)	3	4	3	3
Fever(>38°C) (injection 1; N=81,81,83,82,85,82)	2	5	4	5
Fever(>38°C) (injection 2; N=80,80,81,81,81,82)	2	5	6	5

Notes:

[18] - 81 actually treated as per Safety Set.

End point values	MenB	MenACWY/Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	85	82		
Units: Number of Subjects				
Chills (injection 1; N=81,81,83,82,85,82)	10	14		
Chills (injection 2; N=80,80,81,81,81,82)	8	11		
Malaise (injection 1; N=81,81,83,82,85,82)	8	15		
Malaise (injection 2; N=80,80,81,81,81,82)	15	13		
Myalgia (injection 1; N=81,81,83,82,85,82)	34	31		
Myalgia (injection 2; N=80,80,81,81,81,82)	31	29		
Arthralgia (injection 1; N=81,81,83,82,85,82)	13	12		
Arthralgia (injection 2; N=80,80,81,81,81,82)	12	9		
Headache (injection 1; N=81,81,83,82,85,82)	30	34		
Headache (injection 2 N=80,80,81,81,81,82)	23	28		
Fatigue (injection 1; N=81,81,83,82,85,82)	18	12		
Fatigue (injection 2; N=80,80,81,81,81,82)	9	7		
Nausea (injection 1; N=81,81,83,82,85,82)	8	9		
Nausea (injection 2; N=80,80,81,81,81,82)	7	7		
Rash (injection 1; N=81,81,83,82,85,82)	3	4		
Rash (injection 2; N=80,80,81,81,81,82)	5	2		
Fever(>38°C) (injection 1; N=81,81,83,82,85,82)	2	2		
Fever(>38°C) (injection 2; N=80,80,81,81,81,82)	3	4		

Statistical analyses

No statistical analyses for this end point

Secondary: 13. Number of Subjects who reported Unsolicited AEs during 7 days after each vaccination

End point title	13. Number of Subjects who reported Unsolicited AEs during 7 days after each vaccination

End point description:

Safety was assessed as the number of subjects who reported unsolicited AEs reaction from day 1 through day 7 after each vaccination and SAEs for the entire study period. The data were reported based on the Safety Set.

End point type	Secondary

End point timeframe:

Day 1 through day 7 after each vaccination and Day 1 to day 91 for SAEs.

End point values	MenABCWY	MenAB (X2)CWY	MenABCWY+OMV	MenABCWY+¼OMV
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	80[19]	81	83	82
Units: Number of Subjects				
Any Adverse Events (AEs)	28	28	27	28
At least possibly related AEs	11	11	14	8
Serious Adverse Events (SAEs)	1	0	0	0
At least possibly related SAEs	0	0	0	0

Notes:

[19] - 80 subjects started, 81 were actually analyzed in this group.

End point values	MenB	MenACWY/Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	85	82		
Units: Number of Subjects				
Any Adverse Events (AEs)	27	30		
At least possibly related AEs	6	12		
Serious Adverse Events (SAEs)	2	0		
At least possibly related SAEs	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: 14. Percentage of subjects with hSBA ≥ 1:8 for Serogroups MenA, C, W and Y.

End point title	14. Percentage of subjects with hSBA ≥ 1:8 for Serogroups MenA, C, W and Y.

End point description:

Percentages of subjects with hSBA ≥ 1:8 against N. Meningitidis serogroups A, C, W and Y after the first dose of MenABCWY vaccine. The data were reported based on the PPS.

End point type	Secondary

End point timeframe:

1 month after the 1st vaccination (Day 31).

End point values	MenABCWY	MenAB (X2)CWY	MenABCWY+OMV	MenABCWY+¼OMV
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	79	78	80	81
Units: Percentages of Subjects				
number (confidence interval 95%)				
MenA (Day 31; N=78,78,79,81,78,78)	86 (76 to 93)	88 (79 to 95)	80 (69 to 88)	75 (64 to 84)
MenC (Day 31; N=79,78,80,80,78,79)	85 (75 to 92)	96 (89 to 99)	93 (84 to 97)	93 (84 to 97)
MenW (Day 31; N=79,78,79,80,77,80)	94 (86 to 98)	99 (93 to 100)	100 (95 to 100)	100 (95 to 100)
MenY (Day 31; N=79,78,79,81,78,81)	95 (88 to 99)	92 (84 to 97)	91 (83 to 96)	94 (86 to 98)

End point values	MenB	MenACWY/Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	79	81		
Units: Percentages of Subjects				
number (confidence interval 95%)				
MenA (Day 31; N=78,78,79,81,78,78)	29 (20 to 41)	88 (79 to 95)		
MenC (Day 31; N=79,78,80,80,78,79)	40 (29 to 51)	84 (74 to 91)		
MenW (Day 31; N=79,78,79,80,77,80)	77 (66 to 86)	98 (91 to 100)		
MenY (Day 31; N=79,78,79,81,78,81)	31 (21 to 42)	100 (96 to 100)		

Statistical analyses

No statistical analyses for this end point

Secondary: 15. Percentage of Subjects with hSBA ≥ 1:5 for MenB strains.

End point title	15. Percentage of Subjects with hSBA ≥ 1:5 for MenB strains.

End point description:

Percentages of Subjects with hSBA ≥ 1:5 to N. Meningitidis for the three major meningococcal B Strains (Strain 44/76-SL, Strain 5/99 and Strain NZ98/254). The data were reported based on the PPS.

End point type	Secondary

End point timeframe:

1 month after the 1st vaccination (Day 31).

End point values	MenABCWY	MenAB (X2)CWY	MenABCWY+OMV	MenABCWY+¼OMV
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	79	78	80	81
Units: Percentages of Subjects				
number (confidence interval 95%)				
S.44/76-SL (Day 31; N=79,78,80,80,78,81)	35 (25 to 47)	64 (52 to 75)	66 (55 to 76)	56 (45 to 68)
S.5/99 (Day 31; N=79,78,79,81,78,80)	94 (86 to 98)	99 (93 to 100)	81 (71 to 89)	85 (76 to 92)
S. NZ98/254 (Day 31; N=79,78,80,81,78,80)	4 (1 to 11)	12 (5 to 21)	38 (27 to 49)	30 (21 to 42)

End point values	MenB	MenACWY/Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	79	81		
Units: Percentages of Subjects				
number (confidence interval 95%)				
S.44/76-SL (Day 31; N=79,78,80,80,78,81)	35 (25 to 46)	9 (4 to 18)		
S.5/99 (Day 31; N=79,78,79,81,78,80)	99 (93 to 100)	20 (12 to 30)		
S. NZ98/254 (Day 31; N=79,78,80,81,78,80)	11 (5 to 20)	4 (1 to 10)		

Statistical analyses

No statistical analyses for this end point

Secondary: 16. hSBA GMTs, Serogroups A, C, W and Y.

End point title	16. hSBA GMTs, Serogroups A, C, W and Y.

End point description:

Geometric Mean hSBA Titers (95% CI) for N.Meningitidis Serogroups A, C, W, and Y. The data were reported based on the PPS.

End point type	Secondary

End point timeframe:

1 month after 1st vaccination (Day 31).

End point values	MenABCWY	MenAB (X2)CWY	MenABCWY+OMV	MenABCWY+¼ OMV
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	79	78	80	81
Units: Titers				
geometric mean (confidence interval 95%)				
MenA (Day 31; N=78,78,79,81,78,78)	56 (36 to 85)	73 (48 to 112)	49 (32 to 74)	41 (27 to 62)
MenC (Day 31; N=79,78,80,80,78,79)	54 (39 to 76)	78 (56 to 110)	76 (54 to 107)	82 (58 to 115)
MenW (Day 31; N=79,78,79,80,77,80)	143 (108 to 189)	204 (154 to 270)	183 (138 to 241)	199 (151 to 264)
MenY (Day 31; N=79,78,79,81,78,81)	76 (56 to 103)	77 (57 to 104)	67 (50 to 91)	75 (56 to 101)

End point values	MenB	MenACWY/Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	79	81		
Units: Titers				
geometric mean (confidence interval 95%)				
MenA (Day 31; N=78,78,79,81,78,78)	3.36 (2.2 to 5.14)	105 (68 to 160)		
MenC (Day 31; N=79,78,80,80,78,79)	5.83 (4.14 to 8.2)	59 (42 to 84)		
MenW (Day 31; N=79,78,79,80,77,80)	24 (18 to 32)	188 (142 to 248)		
MenY (Day 31; N=79,78,79,81,78,81)	4.56 (3.38 to 6.16)	77 (57 to 104)		

Statistical analyses

No statistical analyses for this end point

Secondary: 17. hSBA GMTs, Serogroups B strains.

End point title	17. hSBA GMTs, Serogroups B strains.

End point description:

Geometric Mean hSBA Titers (95% CI) for the three major meningococcal B Strains (Strain 44/76-SL, Strain 5/99 and Strain NZ98/254). The data are reported based on the PPS.

End point type	Secondary

End point timeframe:

1 month after 1st vaccination (Day 31).

End point values	MenABCWY	MenAB (X2)CWY	MenABCWY+OMV	MenABCWY+¼ OMV
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	80	79	81	82
Units: Titers				
geometric mean (confidence interval 95%)				
S. 44/76-SL (Day 31; N=79,78,80,80,78,81)	4.22 (3.01 to 5.92)	9.98 (7.1 to 14)	13 (9.06 to 18)	9.03 (6.45 to 13)
S. 5/99 (Day 31; N=79,78,79,81,78,80)	44 (33 to 59)	94 (71 to 124)	24 (18 to 32)	35 (26 to 46)
S. NZ98/254 (Day 31; N=79,78,80,81,78,80)	1.98 (1.59 to 2.46)	2.15 (1.73 to 2.68)	4.9 (3.94 to 6.08)	3.47 (2.8 to 4.31)

End point values	MenB	MenACWY/Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	82	82		
Units: Titers				
geometric mean (confidence interval 95%)				
S. 44/76-SL (Day 31; N=79,78,80,80,78,81)	3.74 (2.67 to 5.25)	1.65 (1.18 to 2.31)		
S. 5/99 (Day 31; N=79,78,79,81,78,80)	72 (54 to 95)	2.26 (1.71 to 2.99)		
S. NZ98/254 (Day 31; N=79,78,80,81,78,80)	1.77 (1.42 to 2.2)	1.71 (1.38 to 2.13)		

Statistical analyses

No statistical analyses for this end point

Secondary: 18. GMRs for Serogroups A, C, W, Y.

End point title	18. GMRs for Serogroups A, C, W, Y.

End point description:

Geometric Mean Ratios for N. meningitides Serogroups A, C, W and Y. The data were reported based on the PPS.

End point type	Secondary

End point timeframe:

1 month after 1st vaccination to pre-vaccination.

End point values	MenABCWY	MenAB (X2)CWY	MenABCWY+OMV	MenABCWY+¼ OMV
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	79	78	80	81
Units: Ratio				
geometric mean (confidence interval 95%)				

MenA (Day 31/day 1; N=78,78,79,80,78,78)	41 (26 to 63)	55 (36 to 85)	38 (24 to 58)	32 (21 to 49)
MenC (Day 31/day 1; N=79,78,80,79,78,78)	12 (8.37 to 18)	20 (14 to 29)	18 (12 to 26)	18 (13 to 27)
MenW (Day 31/day 1; N=79,77,79,78,76,80)	7.8 (5.2 to 12)	12 (7.8 to 18)	10 (6.69 to 15)	11 (7.02 to 16)
MenY (Day 31/day 1; N=79,77,79,81,78,81)	18 (13 to 25)	18 (13 to 26)	16 (11 to 22)	18 (13 to 25)

End point values	MenB	MenACWY/Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	79	81		
Units: Ratio				
geometric mean (confidence interval 95%)				
MenA (Day 31/day 1; N=78,78,79,80,78,78)	2.67 (1.74 to 4.11)	77 (50 to 118)		
MenC (Day 31/day 1; N=79,78,80,79,78,78)	1.3 (0.88 to 1.91)	15 (10 to 22)		
MenW (Day 31/day 1; N=79,77,79,78,76,80)	1.17 (0.77 to 1.77)	10 (7.01 to 16)		
MenY (Day 31/day 1; N=79,77,79,81,78,81)	1.04 (0.75 to 1.46)	15 (11 to 21)		

Statistical analyses

No statistical analyses for this end point

Secondary: 19. GMRs for Serogroups B strains.

End point title	19. GMRs for Serogroups B strains.

End point description:

Geometric Mean Ratio for the three major meningococcal B Strains (Strain 44/76-SL, Strain 5/99 and Strain NZ98/254). The data were reported based on the PPS.

End point type	Secondary

End point timeframe:

1 month after 1st vaccination to pre-vaccination.

End point values	MenABCWY	MenAB (X2)CWY	MenABCWY+OMV	MenABCWY+¼ OMV
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	79	78	80	81
Units: Ratio				
geometric mean (confidence interval 95%)				
S. 44/76-SL (Day 31/day 1; N=79,77,79,79,78,81)	3.36 (2.39 to 4.72)	7.73 (5.49 to 11)	9.81 (6.99 to 14)	7.09 (5.05 to 9.96)
S. 5/99 (Day 31/day 1; N=79,78,79,80,78,80)	19 (14 to 26)	44 (32 to 61)	12 (8.95 to 17)	17 (12 to 23)

S. NZ98 (Day 31/day 1; N=79,78,80,80,78,80)	1.19 (0.95 to 1.49)	1.33 (1.06 to 1.67)	2.91 (2.33 to 3.64)	2.09 (1.67 to 2.61)

End point values	MenB	MenACWY/Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	79	81		
Units: Ratio				
geometric mean (confidence interval 95%)				
S. 44/76-SL (Day 31/day 1; N=79,77,79,79,78,81)	2.9 (2.06 to 4.08)	1.28 (0.91 to 1.79)		
S. 5/99 (Day 31/day 1; N=79,78,79,80,78,80)	29 (21 to 40)	1.02 (0.74 to 1.4)		
S. NZ98 (Day 31/day 1; N=79,78,80,80,78,80)	1.01 (0.8 to 1.26)	1.07 (0.86 to 1.34)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Day 1 to Day 91.	
Adverse event reporting additional description:	
All the unsolicited AEs were reported by non-systematic assessment and the solicited AEs were reported by systemic assessment.	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	17.01

Reporting groups	
Reporting group title	MenABCWY
Reporting group description:	
MenABCWY combination vaccine containing rMenB without outer membrane vesicle (OMV) at a 0, 2-month schedule.	
Reporting group title	MenAB (X2)CWY
Reporting group description:	
MenABCWY combination vaccine containing rMenBx2doses at a 0, 2-month schedule.	
Reporting group title	MenABCWY+OMV
Reporting group description:	
MenABCWY combination vaccine containing rMenB + OMV at 0, 2-month schedule.	
Reporting group title	MenABCWY+¼OMV
Reporting group description:	
MenABCWY combination vaccine containing rMenB + ¼ OMV at 0, 2-month schedule.	
Reporting group title	MenB
Reporting group description:	
rMenB (no OMV) at a 0, 2-month schedule.	
Reporting group title	MenACWY/Placebo
Reporting group description:	
1 dose of MenACWY, 1 dose of placebo at a 0, 2-month schedule.	

Serious adverse events	MenABCWY	MenAB (X2)CWY	MenABCWY+OMV
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 81 (1.23%)	0 / 81 (0.00%)	0 / 83 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Craniocerebral injury			
subjects affected / exposed	0 / 81 (0.00%)	0 / 81 (0.00%)	0 / 83 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			

Intentional product misuse			
subjects affected / exposed	1 / 81 (1.23%)	0 / 81 (0.00%)	0 / 83 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Loss of consciousness			
subjects affected / exposed	0 / 81 (0.00%)	0 / 81 (0.00%)	0 / 83 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	0 / 81 (0.00%)	0 / 81 (0.00%)	0 / 83 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	MenABCWY+¼OMV	MenB	MenACWY/Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 82 (0.00%)	2 / 85 (2.35%)	0 / 82 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Craniocerebral injury			
subjects affected / exposed	0 / 82 (0.00%)	1 / 85 (1.18%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Intentional product misuse			
subjects affected / exposed	0 / 82 (0.00%)	0 / 85 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Loss of consciousness			
subjects affected / exposed	0 / 82 (0.00%)	1 / 85 (1.18%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			

Gastroenteritis			
subjects affected / exposed	0 / 82 (0.00%)	1 / 85 (1.18%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	MenABCWY	MenAB (X2)CWY	MenABCWY+OMV
Total subjects affected by non-serious adverse events			
subjects affected / exposed	73 / 81 (90.12%)	75 / 81 (92.59%)	80 / 83 (96.39%)
Nervous system disorders			
Headache			
subjects affected / exposed	40 / 81 (49.38%)	40 / 81 (49.38%)	48 / 83 (57.83%)
occurrences (all)	69	76	88
General disorders and administration site conditions			
Chills			
subjects affected / exposed	17 / 81 (20.99%)	23 / 81 (28.40%)	22 / 83 (26.51%)
occurrences (all)	27	30	28
Fatigue			
subjects affected / exposed	21 / 81 (25.93%)	16 / 81 (19.75%)	17 / 83 (20.48%)
occurrences (all)	30	23	22
Injection site erythema			
subjects affected / exposed	31 / 81 (38.27%)	35 / 81 (43.21%)	44 / 83 (53.01%)
occurrences (all)	47	47	67
Injection site induration			
subjects affected / exposed	35 / 81 (43.21%)	33 / 81 (40.74%)	48 / 83 (57.83%)
occurrences (all)	47	47	76
Injection site pain			
subjects affected / exposed	70 / 81 (86.42%)	69 / 81 (85.19%)	79 / 83 (95.18%)
occurrences (all)	127	128	151
Injection site swelling			
subjects affected / exposed	18 / 81 (22.22%)	30 / 81 (37.04%)	46 / 83 (55.42%)
occurrences (all)	25	43	72
Malaise			
subjects affected / exposed	22 / 81 (27.16%)	26 / 81 (32.10%)	25 / 83 (30.12%)
occurrences (all)	37	43	33

Pyrexia			
subjects affected / exposed	5 / 81 (6.17%)	10 / 81 (12.35%)	10 / 83 (12.05%)
occurrences (all)	6	12	10
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	18 / 81 (22.22%)	19 / 81 (23.46%)	16 / 83 (19.28%)
occurrences (all)	27	25	23
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	7 / 81 (8.64%)	5 / 81 (6.17%)	6 / 83 (7.23%)
occurrences (all)	9	5	6
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	22 / 81 (27.16%)	18 / 81 (22.22%)	28 / 83 (33.73%)
occurrences (all)	31	25	36
Myalgia			
subjects affected / exposed	48 / 81 (59.26%)	48 / 81 (59.26%)	54 / 83 (65.06%)
occurrences (all)	82	80	91
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	5 / 81 (6.17%)	3 / 81 (3.70%)	6 / 83 (7.23%)
occurrences (all)	5	4	8

Non-serious adverse events	MenABCWY+¼OMV	MenB	MenACWY/Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	76 / 82 (92.68%)	77 / 85 (90.59%)	74 / 82 (90.24%)
Nervous system disorders			
Headache			
subjects affected / exposed	42 / 82 (51.22%)	39 / 85 (45.88%)	42 / 82 (51.22%)
occurrences (all)	70	72	80
General disorders and administration site conditions			
Chills			
subjects affected / exposed	26 / 82 (31.71%)	16 / 85 (18.82%)	21 / 82 (25.61%)
occurrences (all)	36	22	28
Fatigue			
subjects affected / exposed	18 / 82 (21.95%)	23 / 85 (27.06%)	15 / 82 (18.29%)
occurrences (all)	29	31	21

Injection site erythema			
subjects affected / exposed	33 / 82 (40.24%)	29 / 85 (34.12%)	28 / 82 (34.15%)
occurrences (all)	49	42	39
Injection site induration			
subjects affected / exposed	38 / 82 (46.34%)	27 / 85 (31.76%)	26 / 82 (31.71%)
occurrences (all)	55	39	35
Injection site pain			
subjects affected / exposed	76 / 82 (92.68%)	74 / 85 (87.06%)	66 / 82 (80.49%)
occurrences (all)	141	131	106
Injection site swelling			
subjects affected / exposed	29 / 82 (35.37%)	23 / 85 (27.06%)	18 / 82 (21.95%)
occurrences (all)	42	28	29
Malaise			
subjects affected / exposed	27 / 82 (32.93%)	17 / 85 (20.00%)	22 / 82 (26.83%)
occurrences (all)	37	28	32
Pyrexia			
subjects affected / exposed	10 / 82 (12.20%)	5 / 85 (5.88%)	6 / 82 (7.32%)
occurrences (all)	11	5	6
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	16 / 82 (19.51%)	14 / 85 (16.47%)	13 / 82 (15.85%)
occurrences (all)	24	16	16
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	7 / 82 (8.54%)	7 / 85 (8.24%)	6 / 82 (7.32%)
occurrences (all)	7	8	7
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	21 / 82 (25.61%)	22 / 85 (25.88%)	17 / 82 (20.73%)
occurrences (all)	34	29	25
Myalgia			
subjects affected / exposed	50 / 82 (60.98%)	44 / 85 (51.76%)	41 / 82 (50.00%)
occurrences (all)	80	72	67
Infections and infestations			
Nasopharyngitis			

subjects affected / exposed occurrences (all)	5 / 82 (6.10%) 6	11 / 85 (12.94%) 13	9 / 82 (10.98%) 9

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported