Clinical trial results:
A Phase 2, Single-Blind, Controlled, Randomized Study of the Safety, Tolerability and Immunogenicity of Novartis Meningococcal B Recombinant Vaccine ± OMV When Administered at an 0-2-6-Month Schedule in Healthy Adolescents 11-18 Years of Age.

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

Summary

EudraCT number	2014-004734-25
Trial protocol	Outside EU/EEA
Global end of trial date	10 April 2007

Results information

Result version number	v2 (current)
This version publication date	12 June 2016
First version publication date	19 March 2015
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	V72P3

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00297817
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Vaccines and Diagnostics S.r.l
Sponsor organisation address	Via Fiorentina,, Siena, Italy, 53100
Public contact	Posting Director, Novartis Vaccines, RegistryContactVaccinesUS@novartis.com
Scientific contact	Posting Director, Novartis Vaccines, RegistryContactVaccinesUS@novartis.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	06 September 2007
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	10 April 2007
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To explore the immunogenicity of two and three doses of rMenB ± OMV in healthy adolescents at 1 month after the second and third doses, by evaluation of the breadth of bactericidal activity (measured by bactericidal complement assay [BCA]) response against a panel of genetically distinct meningococcal strains.

Protection of trial subjects:

Study vaccines were not administered to individuals with known hypersensitivity to any component of the vaccines. An oral temperature ≥38.0°C (≥100.4°F) or serious active infection was a reason for delaying vaccination. Standard immunization practices were observed and care was taken to administer the injection intramuscularly. As with all injectable vaccines, appropriate medical treatment and supervision was readily available in case of rare anaphylactic reactions following administration of the study vaccine. Epinephrine 1:1000 and diphenhydramine was available in case of any anaphylactic reactions. Care was taken to ensure that the vaccine is not injected into a blood vessel.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 February 2006
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 203
Worldwide total number of subjects	203
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)	15
Adolescents (12-17 years)	172

Adults (18-64 years)	16
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were enrolled from 8 centres in the United States

Pre-assignment

Screening details:

All enrolled subjects were administered the vaccine in accordance with the randomization scheme.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	rMenB

Arm description:

Healthy adolescents 11 through 18 years of age administered three doses of rMenB according to a 0, 2, 6-month immunization schedule

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

Dosage and administration details:

Subjects received 3 doses of 0.5 mL each

Arm title	rMenB + OMV

Arm description:

Healthy adolescents 11 through 18 years of age administered three doses of rMenB + OMV according to a 0, 2, 6-month immunization schedule

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

Dosage and administration details:

Subjects received 3 doses of 0.5 mL each

Arm title	Placebo

Arm description:

Healthy adolescents 11 through 18 years of age administered three doses of placebo according to a 0, 2, 6-month immunization schedule

Arm type	Placebo

Investigational medicinal product name	Saline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 3 doses of 0.5 mL each

Number of subjects in period 1	rMenB	rMenB + OMV	Placebo
Started	83	79	41
Completed	78	76	40
Not completed	5	3	1
Consent withdrawn by subject	3	-	1
Adverse Event	-	2	-
Pregnancy	1	-	-
Lost to follow-up	-	1	-
Inappropriate Enrollment	1	-	-

Baseline characteristics

Reporting groups	
Reporting group title	rMenB
Reporting group description:	
Healthy adolescents 11 through 18 years of age administered three doses of rMenB according to a 0, 2, 6-month immunization schedule	
Reporting group title	rMenB + OMV
Reporting group description:	
Healthy adolescents 11 through 18 years of age administered three doses of rMenB + OMV according to a 0, 2, 6-month immunization schedule	
Reporting group title	Placebo
Reporting group description:	
Healthy adolescents 11 through 18 years of age administered three doses of placebo according to a 0, 2, 6-month immunization schedule	

Reporting group values	rMenB	rMenB + OMV	Placebo
Number of subjects	83	79	41
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	14.3	14.4	14.8
standard deviation	± 2.1	± 1.9	± 2
Gender categorical Units: Subjects			
Female	36	35	18
Male	47	44	23

Reporting group values	Total		
Number of subjects	203		
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)	0		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Age continuous Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical Units: Subjects			
Female	89		
Male	114		

End points

End points reporting groups

Reporting group title	rMenB
Reporting group description:	
Healthy adolescents 11 through 18 years of age administered three doses of rMenB according to a 0, 2, 6-month immunization schedule	
Reporting group title	rMenB + OMV
Reporting group description:	
Healthy adolescents 11 through 18 years of age administered three doses of rMenB + OMV according to a 0, 2, 6-month immunization schedule	
Reporting group title	Placebo
Reporting group description:	
Healthy adolescents 11 through 18 years of age administered three doses of placebo according to a 0, 2, 6-month immunization schedule	
Subject analysis set title	Enrolled population
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All subjects enrolled in the study.	
Subject analysis set title	Modified Intention-to-treat population
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
All randomized subjects who received the vaccine, and provided at least one evaluable serum sample before and one after vaccination	
Subject analysis set title	Per protocol population
Subject analysis set type	Per protocol
Subject analysis set description:	
All subjects in the MITT Set who received all the relevant doses of vaccine correctly, and provided evaluable serum samples at the relevant timepoints, and had no major protocol violation as defined prior to unblinding. A “major” deviation is defined as a protocol deviation that is considered to have a significant impact on the immunogenicity results of the subject compared to the result that would have possibly otherwise been obtained	
Subject analysis set title	Safety population
Subject analysis set type	Safety analysis
Subject analysis set description:	
All subjects who were injected and who had post-injection safety data	

Primary: Percentage of subjects with bactericidal titers ≥1:4 prior to the 1st and at 1 month after the 2nd and 3rd vaccination.

End point title	Percentage of subjects with bactericidal titers ≥1:4 prior to the 1st and at 1 month after the 2nd and 3rd vaccination.[1]
End point description:	
Bactericidal activity as measured by the percentage of subjects achieving BCA titers ≥1:4 against a panel of genetically distinct meningococcal strains (H44/76, 5/99, GB013, NZ98/254) prior to the 1st and 1 month after the 2nd and 3rd doses of either rMenB, rMenB + OMV or placebo	
End point type	Primary
End point timeframe:	
Pre 1st vaccination, 1 month after 2nd vaccination, 1 month after 3rd vaccination	

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: there is no statistical analysis for this endpoint.

End point values	rMenB	rMenB + OMV	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	40	38	23	
Units: Percentage of subjects				
number (confidence interval 95%)				
44/76-SL (Pre 1st vaccination)	3 (0.063 to 13)	11 (3 to 25)	4 (0 to 22)	
44/76-SL (1 month after 2nd vaccination)	98 (87 to 100)	100 (91 to 100)	4 (0 to 22)	
44/76-SL(1 month after 3rd vaccination)N= 38,37,23	100 (91 to 100)	100 (91 to 100)	4 (0 to 22)	
5/99 (Pre 1st vaccination)	5 (1 to 17)	16 (6 to 31)	0 (0 to 15)	
5/99 (1 month after 2nd vaccination)	100 (91 to 100)	100 (91 to 100)	0 (0 to 15)	
5/99(1 month after 3rd vaccination)N=39,37,23	100 (91 to 100)	100 (91 to 100)	0 (0 to 15)	
GB013(Pre 1st vaccination)N=39,38,23	5 (1 to 17)	11 (3 to 25)	4 (0 to 22)	
GB013 (1 month after 2nd vaccination)	20 (9 to 36)	39 (24 to 57)	4 (0 to 22)	
GB013(1 month after 3rd vaccination)N=37,37,23	24 (12 to 41)	54 (37 to 71)	4 (0 to 22)	
NZ98/254(Pre 1st vaccination)N=39,38,23	0 (0 to 9)	8 (2 to 21)	0 (0 to 15)	
NZ98/254(1 month after 2nd vaccination)	10 (3 to 24)	50 (33 to 67)	0 (0 to 15)	
NZ98/254(1 month after 3rd vaccination)N=37,37,23	51 (34 to 68)	76 (59 to 88)	0 (0 to 15)	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of subjects with bactericidal titers ≥1:4 at 4 months after the 2nd and 6 months after the 3rd vaccination

End point title	Percentage of subjects with bactericidal titers ≥1:4 at 4 months after the 2nd and 6 months after the 3rd vaccination[2]

End point description:

Bactericidal activity as measured by the percentage of subjects achieving BCA titers ≥1:4 against a panel of genetically distinct meningococcal strains (H44/76, 5/99, GB013, NZ98/254) at 4 months after the 2nd and 6 months after the 3rd dose of either rMenB, rMenB + OMV or placebo

End point type	Primary

End point timeframe:

4 months after the 2nd vaccination, 6 months after the 3rd vaccination

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: there is no statistical analysis for this endpoint.

End point values	rMenB	rMenB + OMV	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	40	38	23	
Units: Percentage of subjects				
arithmetic mean (confidence interval 95%)				

44/76-SL (4 months after 2nd vaccination)	70 (53 to 83)	87 (72 to 96)	9 (1 to 28)	
44/76-SL(6 months after 3rd vaccination)N=39,38,23	59 (42 to 74)	87 (72 to 96)	9 (1 to 28)	
5/99 (4 months after 2nd vaccination)	100 (91 to 100)	100 (91 to 100)	4 (0 to 22)	
5/99 (6 months after 3rd vaccination)	100 (91 to 100)	100 (91 to 100)	9 (1 to 28)	
GB013 (4 months after 2nd vaccination)	5 (1 to 17)	24 (11 to 40)	0 (0 to 15)	
GB013(6 months after 3rd vaccination)N=39,38,23	8 (2 to 21)	29 (15 to 46)	9 (1 to 28)	
NZ98/254 (4 months after 2nd vaccination)	3 (0.063 to 13)	21 (10 to 37)	0 (0 to 15)	
NZ98/254(6 months after 3rd vaccination)N=39,38,23	3 (0.065 to 13)	18 (8 to 34)	4 (0 to 22)	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of subjects with bactericidal titers ≥1:4 at 7 days after the 3rd vaccination

End point title	Percentage of subjects with bactericidal titers ≥1:4 at 7 days after the 3rd vaccination[3]

End point description:

Bactericidal activity as measured by the percentage of subjects that achieving BCA titers ≥1:4 against a panel of genetically distinct meningococcal strains (H44/76, 5/99, GB013, NZ98/254) at 7 days after the 3rd dose of either rMenB, rMenB + OMV or placebo.

End point type	Primary

End point timeframe:

7 days after the 3rd vaccination

Notes:

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

End point values	rMenB	rMenB + OMV	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	10	6	
Units: Percentage of subjects				
number (confidence interval 95%)				
44/76-SL	89 (52 to 100)	90 (55 to 100)	0 (0 to 46)	
5/99	100 (66 to 100)	90 (55 to 100)	17 (0 to 64)	
GB013	0 (0 to 34)	30 (7 to 65)	17 (0 to 64)	
NZ98/254	22 (3 to 60)	40 (12 to 74)	0 (0 to 46)	

Statistical analyses

No statistical analyses for this end point

Secondary: BCA geometric mean titers prior to the 1st and at 1 month after the 2nd and 3rd vaccination

End point title	BCA geometric mean titers prior to the 1st and at 1 month after the 2nd and 3rd vaccination

End point description:

Bactericidal activity as measured by GMTs against a panel of genetically distinct meningococcal strains (H44/76, 5/99, GB013, NZ98/254) prior to the 1st and 1 month after 2nd and 3rd doses of either rMenB, rMenB + OMV or placebo

End point type	Secondary

End point timeframe:

Pre 1st vaccination, 1 month after 2nd vaccination, 1 month after 3rd vaccination

End point values	rMenB	rMenB + OMV	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	40	38	23	
Units: Titers				
geometric mean (confidence interval 95%)				
44/76-SL (Pre 1st vaccination)	1.06 (0.87 to 1.28)	1.35 (1.11 to 1.64)	1.1 (0.86 to 1.42)	
44/76-SL (1 month after 2nd vaccination)	48 (37 to 62)	102 (78 to 134)	1.1 (0.78 to 1.56)	
44/76-SL(1 month after 3rd vaccination)N=38,37,23	115 (89 to 150)	134 (103 to 175)	1.1 (0.79 to 1.53)	
5/99 (Pre 1st vaccination)	1.23 (0.92 to 1.65)	1.63 (1.21 to 2.2)	1.13 (0.77 to 1.66)	
5/99 (1 month after 2nd vaccination)	359 (288 to 449)	365 (291 to 458)	1.17 (0.88 to 1.56)	
5/99(1 month after 3rd vaccination)N=39,37,23	956 (776 to 1179)	658 (531 to 816)	1.11 (0.85 to 1.46)	
GB013(Pre 1st vaccination)N=39,38,23	1.17 (0.96 to 1.42)	1.31 (1.08 to 1.59)	1.13 (0.88 to 1.45)	
GB013 (1 month after 2nd vaccination)	1.5 (1.12 to 2.01)	3.26 (2.42 to 4.39)	1.13 (0.78 to 1.66)	
GB013(1 month after 3rd vaccination)N=37,37,23	1.63 (1.18 to 2.24)	3.75 (2.72 to 5.16)	1.09 (0.73 to 1.63)	
NZ98/254(Pre 1st vaccination)N=39,38,23	1.04 (0.89 to 1.21)	1.26 (1.08 to 1.46)	1.03 (0.85 to 1.25)	
NZ98/254 (1 month after 2nd vaccination)	1.25 (0.85 to 1.82)	4.62 (3.13 to 6.82)	1.03 (0.62 to 1.69)	
NZ98/254(1 month after 3rd vaccination)N=37,37,23	4.3 (2.74 to 6.75)	9.56 (6.1 to 15)	1.11 (0.63 to 1.94)	

Statistical analyses

No statistical analyses for this end point

Secondary: BCA geometric mean ratio to baseline at 1 month after the second and third vaccination

End point title	BCA geometric mean ratio to baseline at 1 month after the second and third vaccination

End point description:

Bactericidal activity as measured by the ratio between BCA geometric mean titers at 1 months after the 2nd and 3rd doses of either rMenB, rMenB + OMV or placebo and baseline

End point type	Secondary

End point timeframe:

1 month after 2nd vaccination, 1 month after 3rd vaccination

End point values	rMenB	rMenB + OMV	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	40	38	23	
Units: Ratio of GMTs				
geometric mean (confidence interval 95%)				
44/76-SL(1 month after 2nd vacc/prevaccination)	45 (33 to 62)	76 (55 to 104)	1 (0.67 to 1.5)	
44/76-SL(1 month after 3rd vaccination)N=38,37,23	114 (84 to 155)	98 (72 to 134)	0.99 (0.67 to 1.46)	
5/99(1 month after 2nd vacc/prevaccination)	292 (209 to 410)	224 (159 to 315)	1.03 (0.67 to 1.6)	
5/99(1 month after 3rd vaccination)N=39,37,23	777 (542 to 1112)	400 (277 to 579)	0.98 (0.62 to 1.56)	
GB013 (1 month after 2nd vacc/prevaccination)	1.31 (1.04 to 1.65)	2.48 (1.96 to 3.13)	1 (0.74 to 1.35)	
GB013(1 month after 3rd vaccination)N=36,37,23	1.41 (1.08 to 1.83)	2.85 (2.19 to 3.7)	0.96 (0.69 to 1.34)	
NZ98/254 (1 month after 2nd vaccination)	1.21 (0.85 to 1.72)	3.67 (2.57 to 5.25)	1 (0.63 to 1.58)	
NZ98/254(1 month after 3rd vaccination)N=36,37,23	4.38 (2.79 to 6.87)	7.66 (4.91 to 12)	1.07 (0.61 to 1.86)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentages of subjects with four-fold rise in bactericidal titers from baseline at 1 month after the second and third vaccination.

End point title	Percentages of subjects with four-fold rise in bactericidal titers from baseline at 1 month after the second and third vaccination.

End point description:

Bactericidal activity as measured by the percentage of subjects that achieved a four-fold rise in BCA titers at 1 month after the 2nd and 3rd doses of either rMenB, rMenB + OMV or placebo when compared to baseline.

End point type	Secondary

End point timeframe:

1 month after 2nd vaccination, 1 month after 3rd vaccination

End point values	rMenB	rMenB + OMV	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	40	38	23	
Units: Percentage of subjects				
number (confidence interval 95%)				
44/76-SL(1 month after 2nd vaccination)	95 (83 to 99)	97 (86 to 100)	0 (0 to 15)	
44/76-SL(1month after 3rdvaccination)N=39,38,23	100 (91 to 100)	97 (86 to 100)	0 (0 to 15)	
5/99 (1 month after 2nd vaccination)	100 (91 to 100)	100 (91 to 100)	0 (0 to 15)	
5/99 (1 month after 3rd vaccination)	100 (91 to 100)	100 (91 to 100)	0 (0 to 15)	
GB013(1 month after 2nd vaccination)N=39,38,23	3 (0.065 to 13)	16 (6 to 31)	0 (0 to 15)	
GB013(1 month after 3rd vaccination)N=37,38,23	5 (1 to 18)	24 (11 to 40)	0 (0 to 15)	
NZ98/254(1 month after 2nd vaccination)N=39,38,23	10 (3 to 24)	34 (20 to 51)	0 (0 to 15)	
NZ98/254(1 month after 3rd vaccination)N=37,38,23	51 (34 to 68)	58 (41 to 74)	0 (0 to 15)	

Statistical analyses

No statistical analyses for this end point

Secondary: BCA geometric mean titers at 4 month after the 2nd and 6 months after the 3rd vaccination

End point title	BCA geometric mean titers at 4 month after the 2nd and 6 months after the 3rd vaccination

End point description:

Bactericidal activity as measured by GMTs against a panel of genetically distinct meningococcal strains (H44/76, 5/99, GB013, NZ98/254) at 4 months after the 2nd dose and 6 months after the 3rd dose of either rMenB, rMenB + OMV or placebo

End point type	Secondary

End point timeframe:

4 months after the 2nd vaccination, 6 months after the 3rd vaccination

End point values	rMenB	rMenB + OMV	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	40	38	23	
Units: Titers				
geometric mean (confidence interval 95%)				
44/76-SL(4 months after 2nd vaccination)	7.42 (5.04 to 11)	14 (9.12 to 20)	1.32 (0.8 to 2.18)	

44/76-SL(6 months after 3rd vaccination)N=39,38,23	5.25 (3.6 to 7.64)	14 (9.34 to 20)	1.24 (0.76 to 2)	
5/99 (4 months after 2nd vaccination)	122 (89 to 167)	101 (73 to 138)	1.42 (0.94 to 2.13)	
5/99 (6 months after 3rd vaccination)	227 (169 to 304)	135 (101 to 182)	1.38 (0.95 to 2.03)	
GB013 (4 months after 2nd vaccination)	1.22 (0.95 to 1.55)	1.93 (1.51 to 2.46)	1.08 (0.78 to 1.47)	
GB013(6 months after 3rd vaccination)N=39,38,23	1.27 (0.98 to 1.63)	2.13 (1.65 to 2.75)	1.21 (0.87 to 1.68)	
NZ98/254 (4 months after 2nd vaccination)	1.09 (0.82 to 1.44)	2.03 (1.52 to 2.72)	1.04 (0.72 to 1.51)	
NZ98/254(6 months after 3rd vaccination)N=38,39,23	1.12 (0.83 to 1.49)	2.01 (1.5 to 2.69)	1.22 (0.84 to 1.77)	

Statistical analyses

No statistical analyses for this end point

Secondary: BCA geometric mean ratio to baseline at 4 months after the 2nd vaccination and 6 months after the 3rd vaccination

End point title	BCA geometric mean ratio to baseline at 4 months after the 2nd vaccination and 6 months after the 3rd vaccination

End point description:

Bactericidal activity as measured by the ratio between BCA geometric mean titers at 4 months after the 2nd and at 6 months after the 3rd dose of either rMenB, rMenB + OMV or placebo and baseline

End point type	Secondary

End point timeframe:

4 months after the 2nd vaccination, 6 months after the 3rd vaccination

End point values	rMenB	rMenB + OMV	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	40	38	23	
Units: Ratio of GMTs				
geometric mean (confidence interval 95%)				
44/76-SL(4 months after 2nd vacc/prevaccination)	7.02 (4.7 to 10)	10 (6.67 to 15)	1.19 (0.71 to 2.01)	
44/76-SL(6months after 3rdvacc/prevaccn)N=39,38,23	4.97 (3.36 to 7.36)	10 (6.83 to 15)	1.12 (0.68 to 1.86)	
5/99 (4 months after 2nd vacc/prevaccination)	99 (68 to 145)	62 (42 to 91)	1.25 (0.77 to 2.04)	
5/99(6months after 3rdvacc/prevaccn)N=40,38,23	185 (124 to 275)	83 (55 to 125)	1.22 (0.73 to 2.06)	
GB013(4months after 2ndvacc/prevaccn)N=39,38,23	1.05 (0.88 to 1.26)	1.47 (1.22 to 1.77)	0.95 (0.75 to 1.2)	
GB013(6months after 3rdvacc/prevaccn)N=38,38,23	1.09 (0.9 to 1.33)	1.62 (1.34 to 1.97)	1.07 (0.84 to 1.37)	
NZ98/254(4months after 2ndvacc/prevaccn)N=39,38,23	1.05 (0.85 to 1.31)	1.62 (1.3 to 2.01)	1.01 (0.77 to 1.34)	
NZ98/254(6months after 3rdvacc/prevaccn)N=38,38,23	1.12 (0.89 to 1.4)	1.6 (1.28 to 2)	1.18 (0.89 to 1.57)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentages of subjects with four-fold rise in bactericidal titers from baseline at 4 months after the 2nd and 6 months after the 3rd vaccination

End point title	Percentages of subjects with four-fold rise in bactericidal titers from baseline at 4 months after the 2nd and 6 months after the 3rd vaccination

End point description:

Bactericidal activity as measured by the percentage of subjects that achieved a four-fold rise in BCA titers at 4 months after the 2nd dose and at 6 months after the 3rd dose of either rMenB, rMenB+ OMV or placebo when compared to baseline

End point type	Secondary

End point timeframe:

4 months after the 2nd vaccination, 6 months after the 3rd vaccination

End point values	rMenB	rMenB + OMV	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	40	38	23	
Units: Percentage of subjects				
number (confidence interval 95%)				
44/76-SL (4 months after 2nd vaccination)	63 (46 to 77)	66 (49 to 80)	4 (0 to 22)	
44/76-SL(6 months after 3rd vaccination)N=38,37,23	45 (29 to 62)	73 (56 to 86)	4 (0 to 22)	
5/99 (4 months after 2nd vaccination)	100 (91 to 100)	95 (82 to 99)	4 (0 to 22)	
5/99(6 months after 3rd vaccination)N=39,37,23	100 (91 to 100)	95 (82 to 99)	9 (1 to 28)	
GB013(4 months after 2nd vaccination)N=39,38,23	0 (0 to 9)	5 (1 to 18)	0 (0 to 15)	
GB013(6 months after 3rd vaccination)N=37,37,23	0 (0 to 9)	8 (2 to 22)	4 (0 to 22)	
NZ98/254(4 months after 2nd vaccination)N=39,38,23	0 (0 to 9)	11 (3 to 25)	0 (0 to 15)	
NZ98/254(6 months after 3rd vaccination)N=37,37,23	0 (0 to 9)	14 (5 to 29)	4 (0 to 22)	

Statistical analyses

No statistical analyses for this end point

Secondary: BCA geometric mean ratio to pre-3rd vaccination at 6 months after the 3rd vaccination.

End point title	BCA geometric mean ratio to pre-3rd vaccination at 6 months after the 3rd vaccination.

End point description:

Bactericidal activity as measured by the ratio between BCA geometric mean titers at 6 months after the 3rd dose of either rMenB, rMenB + OMV or placebo and pre-3rd vaccination.

End point type	Secondary

End point timeframe:

6 months after the 3rd vaccination

End point values	rMenB	rMenB + OMV	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	40	38	23	
Units: Ratio of GMTs				
geometric mean (confidence interval 95%)				
44/76-SL (N=39,38,23)	0.73 (0.53 to 1.01)	1.01 (0.84 to 1.17)	0.94 (0.62 to 1.43)	
5/99	1.86 (1.28 to 2.7)	1.35 (0.73 to 1.4)	0.98 (0.6 to 1.59)	
GB013 (N=39,38,23)	1.04 (0.87 to 1.24)	1.11 (0.92 to 1.97)	1.13 (0.9 to 1.42)	
NZ98/254 (N=39,38,23)	1.03 (0.87 to 1.22)	0.99 (0.92 to 1.33)	1.17 (0.94 to 1.45)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentages of subjects with four-fold rise in bactericidal titers from pre-3rd vaccination to 6 months after the 3rd vaccination.

End point title	Percentages of subjects with four-fold rise in bactericidal titers from pre-3rd vaccination to 6 months after the 3rd vaccination.

End point description:

Bactericidal activity as measured by the percentage of subjects that achieved a four-fold rise in BCA titers at 6 months after the 3rd dose of either rMenB, rMenB+ OMV or placebo when compared to pre-3rd vaccination

End point type	Secondary

End point timeframe:

6 months after the 3rd vaccination

End point values	rMenB	rMenB + OMV	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	40	38	23	
Units: Percentage of subjects				
number (confidence interval 95%)				
44/76-SL (N=39,38,23)	5 (1 to 17)	5 (1 to 18)	4 (0 to 23)	
5/99	18 (7 to 33)	13 (4 to 28)	9 (1 to 28)	
GB013 (N=39,38,23)	0 (0 to 9)	3 (0.067 to 14)	4 (0 to 22)	
NZ98/254 (N=39,38,23)	0 (0 to 9)	3 (0.067 to 14)	4 (0 to 22)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with bactericidal titers ≥1:4 at 7 days after the 3rd vaccination

End point title	Percentage of subjects with bactericidal titers ≥1:4 at 7 days after the 3rd vaccination

End point description:

Bactericidal activity as measured by the percentage of subjects that achieving BCA titers ≥1:4 against a panel of genetically distinct meningococcal strains (H44/76, 5/99, GB013, NZ98/254) at 7 days after the 3rd dose of either rMenB, rMenB + OMV or placebo.

End point type	Secondary

End point timeframe:

7 days after the 3rd vaccination

End point values	rMenB	rMenB + OMV	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	10	6	
Units: Percentage of subjects				
number (confidence interval 95%)				
44/76-SL	89 (52 to 100)	90 (55 to 100)	0 (0 to 46)	
5/99	100 (66 to 100)	90 (55 to 100)	17 (0 to 64)	
GB013	0 (0 to 34)	30 (7 to 65)	17 (0 to 22)	
NZ98/254	22 (3 to 60)	40 (12 to 74)	0 (0 to 46)	

Statistical analyses

No statistical analyses for this end point

Secondary: BCA geometric mean titers at 7 days after the 3rd vaccination

End point title	BCA geometric mean titers at 7 days after the 3rd vaccination

End point description:

Bactericidal activity as measured by GMTs against a panel of genetically distinct meningococcal strains (H44/76, 5/99, GB013, NZ98/254) at 7 days after the 3rd dose of either rMenB, rMenB + OMV or placebo.

End point type	Secondary

End point timeframe:

7 days after the 3rd vaccination

End point values	rMenB	rMenB + OMV	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	10	6	
Units: Titers				
number (confidence interval 95%)				
44/76-SL	33 (14 to 79)	60 (26 to 137)	1 (0.35 to 2.88)	
5/99	686 (253 to 1858)	367 (142 to 951)	1.26 (0.37 to 4.26)	
GB013	1.05 (0.7 to 1.57)	1.96 (1.33 to 2.89)	1.47 (0.89 to 2.41)	
NZ98/254	1.74 (0.93 to 3.23)	2.76 (1.53 to 4.98)	1 (0.47 to 2.13)	

Statistical analyses

No statistical analyses for this end point

Secondary: BCA geometric mean ratio to baseline at 7 days after the 3rd vaccination.

End point title	BCA geometric mean ratio to baseline at 7 days after the 3rd vaccination.

End point description:

Bactericidal activity as measured by the ratio between BCA geometric mean titers at 7 days after the 3rd dose of either rMenB, rMenB + OMV or placebo and baseline

End point type	Secondary

End point timeframe:

7 days after the 3rd vaccination

End point values	rMenB	rMenB + OMV	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	10	6	
Units: Ratio of GMTs				
geometric mean (confidence interval 95%)				
44/76-SL	33 (14 to 79)	60 (26 to 137)	1 (0.35 to 2.88)	

5/99	697 (245 to 1986)	278 (102 to 754)	1.05 (0.29 to 3.77)	
GB013	1.06 (0.79 to 1.43)	2 (1.5 to 2.67)	0.95 (0.65 to 1.37)	
NZ98/254	1.74 (0.93 to 3.23)	2.76 (1.53 to 4.98)	1 (0.47 to 2.13)	

Statistical analyses

No statistical analyses for this end point

Secondary: ELISA GMCs pre-1st vaccination, at 1 month after the 2nd and 3rd dose, and at 4 months after the 2nd and 6 months after the 3rd vaccination

End point title	ELISA GMCs pre-1st vaccination, at 1 month after the 2nd and 3rd dose, and at 4 months after the 2nd and 6 months after the 3rd vaccination

End point description:

Induction of specific antibody responses against antigens 287-953, 936-741, 961 and OMV-NW as measuring by enzyme-linked immunosorbent assay (ELISA) geometric mean concentrations (GMCs) in subjects receiving either rMenB, rMenB + OMV or placebo.

End point type	Secondary

End point timeframe:

Pre 1st vaccination, at 1 month after the 2nd and 3rd dose, and at 4 months after the 2nd and 6 months after the 3rd vaccination

End point values	rMenB	rMenB + OMV	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	40	38	23	
Units: IU/mL				
geometric mean (confidence interval 95%)				
287-953 antigen Pre 1st vaccination	14 (7.72 to 24)	19 (11 to 35)	13 (5.98 to 26)	
287-953 antigen 1 month after 2nd vaccination	1643 (1120 to 2410)	2847 (1928 to 4204)	11 (6.71 to 18)	
287-953 antigen 4 months after 2nd vaccination	427 (273 to 667)	606 (385 to 954)	11 (6.25 to 20)	
287-953antigen 1month after 3vaccinationN=39,37,23	2945 (2012 to 4310)	3428 (2318 to 5071)	8.42 (5.15 to 14)	
287-953 antigen 6 months after 3rd vaccination	852 (582 to 1247)	1056 (717 to 1558)	18 (11 to 29)	
936-741 antigen Pre 1st vaccination	54 (41 to 71)	82 (62 to 110)	43 (30 to 62)	
936-741 antigen 1 month after 2nd vaccination	5279 (4064 to 6857)	10253 (7857 to 13381)	85 (60 to 120)	
936-741 antigen 4 months after 2nd vaccination	2183 (1663 to 2864)	3305 (2506 to 4358)	76 (53 to 108)	
936-741antigen 1month after 3vaccinationN=39,37,23	13638 (11047 to 16838)	16452 (13249 to 20430)	64 (48 to 83)	
936-741 antigen 6 months after 3rd vaccination	3384 (2708 to 4228)	4388 (3498 to 5505)	63 (47 to 84)	
961 antigen Pre 1st vaccination	100 (73 to 136)	112 (82 to 154)	81 (54 to 122)	

961 antigen 1 month after 2nd vaccination	2133 (1661 to 2738)	2625 (2036 to 3386)	109 (79 to 151)	
961 antigen 4 months after 2nd vaccination	919 (708 to 1194)	839 (643 to 1094)	88 (63 to 124)	
961 antigen1 month after 3vaccinationN=39,37,23	4029 (3263 to 4975)	3757 (3025 to 4666)	83 (63 to 109)	
961 antigen 6 months after 3rd vaccination	1845 (1504 to 2263)	1437 (1167 to 1769)	144 (110 to 188)	
OMV-NW Pre 1st vaccination	4.29 (2.87 to 6.4)	7.3 (4.86 to 11)	5.36 (3.18 to 9.03)	
OMV-NW 1 month after 2nd vaccination	8.64 (5.58 to 13)	522 (334 to 814)	6.42 (3.63 to 11)	
OMV-NW 4 months after 2nd vaccination	15 (11 to 22)	103 (71 to 150)	12 (7.19 to 19)	
OMV-NW 1month after 3vaccinationN=39,37,23	27 (17 to 42)	644 (402 to 1030)	13 (7.14 to 23)	
OMV-NW 6 months after 3rd vaccination	26 (18 to 39)	142 (95 to 213)	21 (13 to 35)	

Statistical analyses

No statistical analyses for this end point

Secondary: ELISA GMCs at 7 days after the 3rd vaccination.

End point title	ELISA GMCs at 7 days after the 3rd vaccination.

End point description:

Induction of specific antibody responses against antigens 287-953, 936-741, 961 and OMV-NW as measuring by enzyme-linked immunosorbent assay (ELISA) geometric mean concentrations (GMCs) in subjects receiving either rMenB, rMenB + OMV or placebo

End point type	Secondary

End point timeframe:

7 days after 3rd vaccination

End point values	rMenB	rMenB + OMV	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	10	6	
Units: IU/mL				
geometric mean (confidence interval 95%)				
287-953 antigen	1316 (450 to 3843)	1455 (523 to 4046)	3.36 (0.91 to 12)	
936-741 antigen	9325 (3020 to 28790)	6161 (2101 to 18065)	57 (14 to 226)	
961 antigen	3114 (1608 to 6031)	1912 (1017 to 3592)	91 (40 to 203)	
OMV-NW	14 (4.44 to 42)	157 (54 to 457)	20 (5.02 to 78)	

Statistical analyses

No statistical analyses for this end point

Secondary: Incidences of (severe) local and systemic reactions during the 7 days following the 1st vaccination

End point title	Incidences of (severe) local and systemic reactions during the 7 days following the 1st vaccination

End point description:

Safety and tolerability of rMenB and rMenB + OMV in healthy adolescents relative to a placebo control arm in terms of number of subjects that experienced (severe) local or systemic solicited adverse events (AEs) or other indicators of reactogenicity during the 7 days following the 1st vaccination

End point type	Secondary

End point timeframe:

Day 1 through Day 7

End point values	rMenB	rMenB + OMV	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	83	79	41	
Units: Subjects				
Injection site pain	74	76	9	
Severe injection site pain	6	12	0	
Erythema	9	30	6	
Severe erythema	0	0	0	
Induration	4	18	0	
Severe induration	0	0	0	
Fever	1	0	0	
Severe fever	0	0	0	
Chills	15	10	5	
Severe chills	1	0	0	
Nausea	16	18	8	
Severe Nausea	1	2	2	
Malaise	24	25	8	
Severe malaise	1	3	2	
Fatigue	27	29	12	
Severe fatigue	1	2	1	
Myalgia	23	21	5	
Severe myalgia	0	1	1	
Arthralgia	12	9	5	
Severe arthralgia	0	0	1	
Headache	32	30	12	
Severe headache	3	0	1	
Stayed home due to reaction	5	5	1	
Analgesic/antipyretic medication use	23	31	6	

Statistical analyses

No statistical analyses for this end point

Secondary: Incidences of (severe) local and systemic reactions during the 7 days following the 2nd vaccination

End point title	Incidences of (severe) local and systemic reactions during the 7 days following the 2nd vaccination

End point description:

To explore the safety and tolerability of rMenB and rMenB + OMV in healthy adolescents relative to a placebo control arm in terms of number of subjects that experienced (severe) local, or systemic solicited adverse events (AEs) or other indicators of reactogenicity during the 7 days following the 2nd vaccination

End point type	Secondary

End point timeframe:

Day 61 through Day 67

End point values	rMenB	rMenB + OMV	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	81	77	41	
Units: Subjects				
Injection site pain	60	67	10	
Severe injection site pain	5	12	1	
Erythema	17	26	8	
Severe erythema	0	0	0	
Induration	11	21	4	
Severe induration	0	0	0	
Fever	0	1	0	
Severe fever	0	0	0	
Chills	9	11	2	
Severe chills	0	3	0	
Nausea	11	8	3	
Severe Nausea	0	2	1	
Malaise	16	18	4	
Severe malaise	0	4	1	
Fatigue	28	25	9	
Severe fatigue	1	3	1	
Myalgia	16	20	2	
Severe myalgia	0	2	1	
Arthralgia	9	17	4	
Severe arthralgia	0	2	0	
Headache	21	20	7	
Severe headache	1	5	1	
Stayed home due to reaction	1	5	0	
Analgesic/antipyretic medication use	14	21	4	

Statistical analyses

No statistical analyses for this end point

Secondary: Incidences of (severe) local and systemic reactions during the 7 days following the 3rd vaccination

End point title	Incidences of (severe) local and systemic reactions during the 7 days following the 3rd vaccination

End point description:

To explore the safety and tolerability of rMenB and rMenB + OMV in healthy adolescents relative to a placebo control arm in terms of number of subjects that experienced (severe) local, or systemic solicited adverse events (AEs) or other indicators of reactogenicity during the 7 days following the 3rd vaccination.

End point type	Secondary

End point timeframe:

Day 181 through Day 187

End point values	rMenB	rMenB + OMV	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	78	76	40	
Units: Subjects				
Injection site pain	57	66	6	
Severe injection site pain	6	13	0	
Erythema	21	23	2	
Severe erythema	1	0	0	
Induration	20	25	0	
Severe induration	0	0	0	
Fever	1	0	1	
Severe fever	0	0	0	
Chills	4	9	2	
Severe chills	0	1	0	
Nausea	1	7	5	
Severe Nausea	1	0	0	
Malaise	10	18	6	
Severe malaise	3	3	0	
Fatigue	21	13	7	
Severe fatigue	1	5	1	
Myalgia	13	13	4	
Severe myalgia	0	3	0	
Arthralgia	6	8	2	
Severe arthralgia	0	2	0	
Headache	12	17	6	
Severe headache	2	1	0	
Stayed home due to reaction	1	1	0	
Analgesic/antipyretic medication use	11	16	3	

Statistical analyses

No statistical analyses for this end point

Secondary: Overview of other unsolicited AEs

End point title	Overview of other unsolicited AEs

End point description:

To explore the safety and tolerability of rMenB and rMenB + OMV in healthy adolescents relative to a placebo control arm in terms of number of subjects that experienced other unsolicited AEs after any vaccination, including possible/probable relationship to the vaccine administered

End point type	Secondary

End point timeframe:

Day 1 through study termination

End point values	rMenB	rMenB + OMV	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	83	79	41	
Units: Number of subjects				
AE including abnormal laboratory values	82	78	41	
AE when excluding abnormal laboratory values	60	50	26	
Atleast possible AE including abnormal lab values	22	25	4	
AEs leading to withdrawal from the study	0	2	0	
SAE including abnormal laboratory values	0	1	2	
Atleast possible related SAE abnormal lab values	0	1	0	
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 AEs, oral temperature, all other AEs, and all concomitant medications were collected for 7 days following each vaccination. SAEs and AEs leading to withdrawal from the study were collected throughout the entire study period.

Adverse event reporting additional description:

Solicited local and systemic AEs, oral temperature, all other AEs, and all concomitant medications were collected for 7 days following each vaccination through systematic assessment. SAEs and AEs leading to withdrawal from the study were collected throughout the entire study period through non-systematic assessment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	9.1

Reporting groups

Reporting group title	rMenB

Reporting group description:

Healthy adolescents 11 through 18 years of age administered three doses of rMenB according to a 0, 2, 6-month immunization schedule

Reporting group title	Placebo

Reporting group description:

Healthy adolescents 11 through 18 years of age administered three doses of placebo according to a 0, 2, 6-month immunization schedule

Reporting group title	rMenB + OMV

Reporting group description:

Healthy adolescents 11 through 18 years of age administered three doses of rMenB + OMV according to a 0, 2, 6-month immunization schedule

Serious adverse events	rMenB	Placebo	rMenB + OMV
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 83 (0.00%)	2 / 41 (4.88%)	1 / 79 (1.27%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
ALCOHOL POISONING			
subjects affected / exposed	0 / 83 (0.00%)	1 / 41 (2.44%)	0 / 79 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
APPENDICITIS			

subjects affected / exposed	0 / 83 (0.00%)	0 / 41 (0.00%)	1 / 79 (1.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PELVIC INFLAMMATORY DISEASE			
subjects affected / exposed	0 / 83 (0.00%)	1 / 41 (2.44%)	0 / 79 (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	rMenB	Placebo	rMenB + OMV
Total subjects affected by non-serious adverse events			
subjects affected / exposed	83 / 83 (100.00%)	41 / 41 (100.00%)	79 / 79 (100.00%)
Investigations			
ACTIVATED PARTIAL THROMBOPLASTIN TIME PROLONGED			
subjects affected / exposed	4 / 83 (4.82%)	1 / 41 (2.44%)	5 / 79 (6.33%)
occurrences (all)	6	1	19
ALANINE AMINOTRANSFERASE DECREASED			
subjects affected / exposed	20 / 83 (24.10%)	9 / 41 (21.95%)	13 / 79 (16.46%)
occurrences (all)	42	16	26
ALANINE AMINOTRANFERASE INCREASED			
subjects affected / exposed	8 / 83 (9.64%)	3 / 41 (7.32%)	3 / 79 (3.80%)
occurrences (all)	13	3	4
BLOOD ALKALINE PHOSPHATASE INCREASED			
subjects affected / exposed	3 / 83 (3.61%)	1 / 41 (2.44%)	4 / 79 (5.06%)
occurrences (all)	7	2	13
BLOOD BICARBONATE DECREASED			
subjects affected / exposed	7 / 83 (8.43%)	4 / 41 (9.76%)	8 / 79 (10.13%)
occurrences (all)	11	4	9
BLOOD BILIRUBIN DECREASED			
subjects affected / exposed	3 / 83 (3.61%)	2 / 41 (4.88%)	5 / 79 (6.33%)
occurrences (all)	5	2	8
BLOOD BILIRUBIN INCREASED			

subjects affected / exposed	1 / 83 (1.20%)	3 / 41 (7.32%)	0 / 79 (0.00%)
occurrences (all)	3	5	0
BLOOD CHLORIDE INCREASED			
subjects affected / exposed	1 / 83 (1.20%)	0 / 41 (0.00%)	4 / 79 (5.06%)
occurrences (all)	1	0	4
BLOOD CREATINE PHOSPHOKINASE INCREASED			
subjects affected / exposed	4 / 83 (4.82%)	2 / 41 (4.88%)	11 / 79 (13.92%)
occurrences (all)	6	2	19
BLOOD CREATININE INCREASED			
subjects affected / exposed	4 / 83 (4.82%)	4 / 41 (9.76%)	8 / 79 (10.13%)
occurrences (all)	6	4	14
BLOOD FIBRINOGEN INCREASED			
subjects affected / exposed	2 / 83 (2.41%)	1 / 41 (2.44%)	5 / 79 (6.33%)
occurrences (all)	4	1	8
BLOOD GLUCOSE INCREASED			
subjects affected / exposed	7 / 83 (8.43%)	3 / 41 (7.32%)	5 / 79 (6.33%)
occurrences (all)	10	5	5
BLOOD LACTATE DEHYDROGENASE INCREASED			
subjects affected / exposed	5 / 83 (6.02%)	1 / 41 (2.44%)	0 / 79 (0.00%)
occurrences (all)	7	1	0
EOSINOPHIL COUNT INCREASED			
subjects affected / exposed	6 / 83 (7.23%)	4 / 41 (9.76%)	3 / 79 (3.80%)
occurrences (all)	8	4	5
FIBRIN D DIMER INCREASED			
subjects affected / exposed	1 / 83 (1.20%)	3 / 41 (7.32%)	2 / 79 (2.53%)
occurrences (all)	2	7	2
HAEMATOCRIT INCREASED			
subjects affected / exposed	46 / 83 (55.42%)	23 / 41 (56.10%)	41 / 79 (51.90%)
occurrences (all)	108	54	100
HAEMOGLOBIN DECREASED			
subjects affected / exposed	3 / 83 (3.61%)	0 / 41 (0.00%)	4 / 79 (5.06%)
occurrences (all)	3	0	7
HAEMOGLOBIN INCREASED			

subjects affected / exposed	17 / 83 (20.48%)	11 / 41 (26.83%)	19 / 79 (24.05%)
occurrences (all)	33	18	40
LYMPHOCYTE COUNT DECREASED			
subjects affected / exposed	30 / 83 (36.14%)	20 / 41 (48.78%)	33 / 79 (41.77%)
occurrences (all)	57	41	68
LYMPHOCYTE COUNT INCREASED			
subjects affected / exposed	25 / 83 (30.12%)	8 / 41 (19.51%)	26 / 79 (32.91%)
occurrences (all)	56	14	70
MEAN CELL HAEMOGLOBIN DECREASED			
subjects affected / exposed	4 / 83 (4.82%)	1 / 41 (2.44%)	4 / 79 (5.06%)
occurrences (all)	13	5	8
MEAN CELL VOLUME INCREASED			
subjects affected / exposed	16 / 83 (19.28%)	10 / 41 (24.39%)	19 / 79 (24.05%)
occurrences (all)	31	18	32
MONOCYTE COUNT INCREASED			
subjects affected / exposed	14 / 83 (16.87%)	7 / 41 (17.07%)	11 / 79 (13.92%)
occurrences (all)	28	11	21
NEUTROPHIL COUNT DECREASED			
subjects affected / exposed	4 / 83 (4.82%)	2 / 41 (4.88%)	6 / 79 (7.59%)
occurrences (all)	4	2	13
NEUTROPHIL COUNT INCREASED			
subjects affected / exposed	35 / 83 (42.17%)	20 / 41 (48.78%)	35 / 79 (44.30%)
occurrences (all)	65	44	80
PLATELET COUNT DECREASED			
subjects affected / exposed	3 / 83 (3.61%)	3 / 41 (7.32%)	6 / 79 (7.59%)
occurrences (all)	3	5	8
PLATELET COUNT INCREASED			
subjects affected / exposed	9 / 83 (10.84%)	3 / 41 (7.32%)	3 / 79 (3.80%)
occurrences (all)	11	5	5
RED BLOOD CELL COUNT INCREASED			
subjects affected / exposed	15 / 83 (18.07%)	9 / 41 (21.95%)	16 / 79 (20.25%)
occurrences (all)	30	18	29
PROTHROMBIN TIME PROLONGED			

subjects affected / exposed	4 / 83 (4.82%)	1 / 41 (2.44%)	5 / 79 (6.33%)
occurrences (all)	14	4	9
WHITE BLOOD CELL COUNT DECREASED			
subjects affected / exposed	25 / 83 (30.12%)	10 / 41 (24.39%)	25 / 79 (31.65%)
occurrences (all)	46	15	51
Nervous system disorders			
HEADACHE			
subjects affected / exposed	44 / 83 (53.01%)	17 / 41 (41.46%)	42 / 79 (53.16%)
occurrences (all)	97	36	82
General disorders and administration site conditions			
CHILLS			
subjects affected / exposed	22 / 83 (26.51%)	6 / 41 (14.63%)	20 / 79 (25.32%)
occurrences (all)	32	14	36
FATIGUE			
subjects affected / exposed	42 / 83 (50.60%)	17 / 41 (41.46%)	42 / 79 (53.16%)
occurrences (all)	100	39	88
INJECTION SITE ERYTHEMA			
subjects affected / exposed	30 / 83 (36.14%)	11 / 41 (26.83%)	49 / 79 (62.03%)
occurrences (all)	49	17	83
INJECTION SITE INDURATION			
subjects affected / exposed	27 / 83 (32.53%)	4 / 41 (9.76%)	39 / 79 (49.37%)
occurrences (all)	37	4	72
INJECTION SITE PAIN			
subjects affected / exposed	78 / 83 (93.98%)	16 / 41 (39.02%)	77 / 79 (97.47%)
occurrences (all)	197	28	227
MALAISE			
subjects affected / exposed	30 / 83 (36.14%)	12 / 41 (29.27%)	36 / 79 (45.57%)
occurrences (all)	66	23	80
Immune system disorders			
MEAN CELL HAEMOGLOBIN CONCENTRATION DECREASED			
subjects affected / exposed	53 / 83 (63.86%)	28 / 41 (68.29%)	54 / 79 (68.35%)
occurrences (all)	110	61	111
Gastrointestinal disorders			
NAUSEA			

subjects affected / exposed	21 / 83 (25.30%)	10 / 41 (24.39%)	23 / 79 (29.11%)
occurrences (all)	37	23	40
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	24 / 83 (28.92%)	6 / 41 (14.63%)	23 / 79 (29.11%)
occurrences (all)	34	15	39
MYALGIA			
subjects affected / exposed	37 / 83 (44.58%)	7 / 41 (17.07%)	35 / 79 (44.30%)
occurrences (all)	61	22	64
Infections and infestations			
SINUSITIS			
subjects affected / exposed	6 / 83 (7.23%)	0 / 41 (0.00%)	5 / 79 (6.33%)
occurrences (all)	6	0	5
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	4 / 83 (4.82%)	4 / 41 (9.76%)	8 / 79 (10.13%)
occurrences (all)	7	4	12

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 January 2006	The evaluation of immunogenicity measured as breadth of BCA and ELISA in a subgroup of subjects 7 days after the third dose was added. It was added that a subgroup of 15 consecutive subjects enrolled at sites 01, 03, and 08 were to provide samples for additional clinical laboratory safety testing including coagulation tests according to the Time and Events Table. This subgroup was to have extended chemistry laboratory evaluations performed at baseline and 7 days after each injection and provide serology samples 7 days after the third injection. The clinical lab safety tests should include PT, INR, PTT, fibrinogen and D-dimer coagulation tests. To provide stopping rules pertaining to clinical laboratory evaluations the following sentence was added: "In the event that any clinical laboratory value is in the alert range and is thought to be related to study vaccine, the study will temporarily be halted." To exclude a medication known to affect liver function testing the following exclusion criterion was added: "are currently receiving or have received Accutane (Isotretinoin) in the previous 14 days". The amount of NaCl in the rMenB + OMV vaccine was corrected to 3 mg per 0.5 mL dose. It was clarified that abnormal clinical lab results were not to be graded as mild, moderate or severe. The criteria for assessing safety objectives were inadvertently not included in the original protocol and were therefore added in the amendment

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported