Clinical trial results:
A Phase 2, Single Blind, Single Center, Randomized Study of the Safety, Tolerability and Immunogenicity of Novartis Meningococcal B Recombinant Vaccine +/- OMV, when Administered to Healthy Infants 6-8 months old

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

Summary

EudraCT number	2006-005589-38
Trial protocol	GB
Global end of trial date	15 July 2008

Results information

Result version number	v2 (current)
This version publication date	15 June 2016
First version publication date	08 January 2015
Version creation reason	• Correction of full data set Data points need to be updated.

Trial information

Trial identification

Sponsor protocol code	V72P9

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00433914
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Vaccines and Diagnostics S.r.l
Sponsor organisation address	S.r.l. - via Fiorentina 1, Siena, Italy, 53100
Public contact	Posting Director, Novartis Vaccines and Diagnostics S.r.l., RegistryContactVaccinesUS@novartis.com
Scientific contact	Posting Director, Novartis Vaccines and Diagnostics S.r.l., 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-000139-PIP01-07
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	24 February 2009
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	15 July 2008
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To explore the immunogenicity of Novartis rMenB Vaccine +/- OMV when administered to healthy infants, at 30 days after the second and the third dose, by evaluation of the breadth of bactericidal activity (BCA) response against a panel of genetically distinct meningococcal strains.

To explore the safety and tolerability of Novartis rMenB with or without OMV throughout the clinical study.

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	16 February 2007
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	6 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 60
Worldwide total number of subjects	60
EEA total number of subjects	60

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	60
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were enrolled at one study center in the UK.

Pre-assignment

Screening details:

All subjects enrolled were included in the trial.

Period 1

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

Blinding implementation details:

The trial was designed as a single-blind study with the study personnel being aware of the vaccine administered, but the enrolled subjects and their parents unaware of the vaccine received.

Arms

Are arms mutually exclusive?	Yes
Arm title	rMenB

Arm description:

6-8 month-old infants were administered 3 doses of Novartis rMenB vaccine without OMV-NZ at 6-8 months of age, 2 months later and at 12 months of age.

Arm type	Experimental
Investigational medicinal product name	Novartis rMenB vaccine
Investigational medicinal product code	
Other name	Serogroup B meningococcal recombinant vaccine without OMV-NZ
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Vaccination consisted of three 0.5 mL doses of rMenB vaccine administered IM into anterolateral area of the right thigh

Arm title	rMenB + OMV

Arm description:

6-8 month-old infants were administered 3 doses of Novartis rMenB with OMV-NZ vaccine at 6-8 months of age, 2 months later and at 12 months of age.

Arm type	Experimental
Investigational medicinal product name	Novartis rMenB + OMV
Investigational medicinal product code	
Other name	Serogroup B meningococcal recombinant vaccine with OMV-NZ
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Vaccination consisted of three 0.5 mL doses of rMenB + OMV vaccine administered IM into anterolateral area of the right thigh

Number of subjects in period 1	rMenB	rMenB + OMV
Started	30	30
Completed	30	27
Not completed	0	3
Consent withdrawn by subject	-	2
Lost to follow-up	-	1

Baseline characteristics

Reporting groups	
Reporting group title	rMenB
Reporting group description:	
6-8 month-old infants were administered 3 doses of Novartis rMenB vaccine without OMV-NZ at 6-8 months of age, 2 months later and at 12 months of age.	
Reporting group title	rMenB + OMV
Reporting group description:	
6-8 month-old infants were administered 3 doses of Novartis rMenB with OMV-NZ vaccine at 6-8 months of age, 2 months later and at 12 months of age.	

Reporting group values	rMenB	rMenB + OMV	Total
Number of subjects	30	30	60
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	30	30	60
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
6-8 month-old infants were administered 3 doses of Novartis rMenB vaccine with or without OMV-NZ at 6-8, 2 months later and at 12 months of age.			
Units: months			
arithmetic mean	228.1	230.1	
standard deviation	± 18	± 19.4	-
Gender categorical			
6-8 month-old infants were administered 3 doses of Novartis rMenB vaccine with or without OMV-NZ at 6-8, 2 months later and at 12 months of age.			
Units: Subjects			
Female	14	18	32
Male	16	12	28

End points

End points reporting groups

Reporting group title	rMenB

Reporting group description:

6-8 month-old infants were administered 3 doses of Novartis rMenB vaccine without OMV-NZ at 6-8 months of age, 2 months later and at 12 months of age.

Reporting group title	rMenB + OMV

Reporting group description:

6-8 month-old infants were administered 3 doses of Novartis rMenB with OMV-NZ vaccine at 6-8 months of age, 2 months later and at 12 months of age.

Subject analysis set title	All enrolled population
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All subjects who had data in the DEMOG panel.

Subject analysis set title	Per-protocol Populatoin
Subject analysis set type	Per protocol

Subject analysis set description:

All enrolled subjects who correctly received the vaccine, provided evaluable serum samples at the relevant time points (Visit 3), and had no major protocol violation as defined prior to the end of the study.

Subject analysis set title	Safety Population
Subject analysis set type	Safety analysis

Subject analysis set description:

All subjects who received the study vaccine and provided some post-vaccination safety data

Primary: Percentage of Subjects With Bactericidal Titers ≥1:4 Against Meningococcal Strains One Month After Second and Third Vaccination of rMenB Vaccine With and Without OMV-NZ

End point title	Percentage of Subjects With Bactericidal Titers ≥1:4 Against Meningococcal Strains One Month After Second and Third Vaccination of rMenB Vaccine With and Without OMV-NZ[1]

End point description:

Immunogenicity was measured as the percentage of subjects who achieved bactericidal titers ≥1:4 against meningococcal strains 44/76-SL, 5/99, NZ98/254 evaluated using serum bactericidal assay, before vaccination (baseline) and one month after second vaccination (2 months after vaccination at 6-8 months) and third vaccination (at 12 months of age).
The analysis was performed on the per-protocol population.

End point type	Primary

End point timeframe:

Baseline and one month after second and third 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: No statistical analyses for this end point.

End point values	rMenB	rMenB + OMV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	24		
Units: Percentage of subjects				
number (confidence interval 95%)				
Strain 44/76-SL - Baseline	8 (1 to 26)	29 (13 to 51)		

Strain 44/76-SL - Post- 2nd vaccination (N=25,23)	100 (86 to 100)	100 (85 to 100)		
Strain 44/76-SL - Post-3rd vaccination (N=24,24)	100 (86 to 100)	100 (86 to 100)		
Strain 5/99 - Baseline	0 (0 to 14)	0 (0 to 14)		
Strain 5/99 - Post-2nd vaccination (N=25,23)	100 (86 to 100)	100 (85 to 100)		
Strain 5/99 - Post-3rd vaccination (N=24,24)	100 (86 to 100)	100 (86 to 100)		
Strain NZ98/254 - Baseline	0 (0 to 14)	0 (0 to 14)		
Strain NZ98/254 - Post-2nd vaccination (N=24,22)	4 (0 to 21)	95 (77 to 100)		
Strain NZ98/254 - Post-3rd vaccination (N=22,24)	9 (1 to 29)	96 (79 to 100)		
Strain UK P1.7-2,4 -Baseline (N=24,21)	0 (0 to 14)	0 (0 to 16)		
Strain UKP1.7-2,4 - Post-2nd vaccination (N=23,19)	0 (0 to 15)	100 (82 to 100)		
Strain UKP1.7-2,4 - Post-3rd vaccination (N=21,22)	5 (0 to 24)	100 (85 to 100)		
Strain GB101 - Baseline (N=24,21)	0 (0 to 14)	10 (1 to 30)		
Strain GB101 - Post-2nd vaccination (N=22,21)	23 (8 to 45)	67 (43 to 85)		
Strain GB101 - Post-3rd vaccination (N=22,22)	27 (11 to 50)	73 (50 to 89)		
Strain GB355 - Baseline (N=12,11)	0 (0 to 26)	0 (0 to 28)		
Strain GB355 - Post-2nd vaccination (N=11,14)	0 (0 to 28)	7 (0 to 34)		
Strain GB355 – Post 3rd vaccination (N=12,11)	0 (0 to 26)	18 (2 to 52)		
Strain GB364 - Baseline (N=22,17)	9 (1 to 29)	12 (1 to 36)		
Strain GB364 - Post-2nd vaccination (N=19,16)	95 (74 to 100)	88 (62 to 98)		
Strain GB364 - Post-3rd vaccination (N=17,19)	88 (64 to 99)	95 (74 to 100)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Bactericidal Titers ≥1:8 Against Meningococcal Strains One Month After Second and Third Vaccination of rMenB Vaccine With and Without OMV-NZ

End point title	Percentage of Subjects With Bactericidal Titers ≥1:8 Against Meningococcal Strains One Month After Second and Third Vaccination of rMenB Vaccine With and Without OMV-NZ[2]

End point description:

Immunogenicity was measured as the percentage of subjects who achieved bactericidal titers ≥1:8 against meningococcal strains 44/76-SL, 5/99, NZ98/254 before vaccination (baseline) and one month after second vaccination (2 months after vaccination at 6-8 months) and third vaccination (at 12 months of age).
The analysis was performed on the per-protocol population.

End point type	Primary

End point timeframe:

Baseline and one month after second and third 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: No statistical analyses for this end point.

End point values	rMenB	rMenB + OMV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	24		
Units: Percentage of subjects				
number (confidence interval 95%)				
Strain 44/76-SL - Baseline	0 (0 to 14)	4 (0 to 21)		
Strain 44/76-SL - Post- 2nd Vaccination (N=25,23)	96 (80 to 100)	100 (85 to 100)		
Strain 44/76-SL - Post-3rd Vaccination (N=24,24)	100 (86 to 100)	100 (86 to 100)		
Strain 5/99 - Baseline	0 (0 to 14)	0 (0 to 14)		
Strain 5/99 - Post-2nd Vaccination (N=25,23)	100 (86 to 100)	100 (85 to 100)		
Strain 5/99 - Post-3rd Vaccination (N=24,24)	100 (86 to 100)	100 (86 to 100)		
Strain NZ98/254 - Baseline	0 (0 to 14)	0 (0 to 14)		
Strain NZ98/254 - Post- 2nd Vaccination (N=24,22)	0 (0 to 14)	91 (71 to 99)		
Strain NZ98/254 - Post- 3rd Vaccination (N=22,24)	5 (0 to 23)	96 (79 to 100)		
Strain UK P1.7-2,4 - Baseline (N=24,21)	0 (0 to 14)	0 (0 to 16)		
Strain UKP1.7-2,4 - Post- 2nd Vaccination (N=23,19	0 (0 to 15)	84 (60 to 97)		
Strain UKP1.7-2,4 - Post- 3rd Vaccination (N=21,22	0 (0 to 16)	95 (77 to 100)		
Strain GB101 – Baseline (N=24,21)	0 (0 to 14)	10 (1 to 30)		
Strain GB101 - Post-2nd Vaccination (N=22,21)	9 (1 to 29)	33 (15 to 57)		
Strain GB101 - Post-3rd Vaccination (N=22,22)	14 (3 to 35)	45 (24 to 68)		
Strain GB355 – Baseline (N=12,11)	0 (0 to 26)	0 (0 to 28)		
Strain GB355 - Post-2nd Vaccination (N=11,14)	0 (0 to 28)	0 (0 to 23)		
Strain GB355 – Post 3rd Vaccination (N=12,11)	0 (0 to 26)	0 (0 to 28)		
Strain GB364 – Baseline (N=22,17)	0 (0 to 15)	0 (0 to 20)		
Strain GB364 - Post-2nd Vaccination (N=19,16)	74 (49 to 91)	69 (41 to 89)		
Strain GB364 - Post-3rd Vaccination (N=17,19)	71 (44 to 90)	84 (60 to 97)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Four-fold Rise in Bactericidal Titers Against Meningococcal Strains One Month After Second and Third Vaccination of rMenB Vaccine With and Without OMV-NZ

End point title	Percentage of Subjects With Four-fold Rise in Bactericidal Titers Against Meningococcal Strains One Month After Second and

	Third Vaccination of rMenB Vaccine With and Without OMV-NZ

End point description:

Immunogenicity was measured as the percentage of subjects who achieved a four-fold increase in bactericidal titers against meningococcal strains 44/76-SL, 5/99, NZ98/254, one month after second vaccination (2 months after vaccination at 6-8 months) and third vaccination (at 12 months of age). The analysis was performed on the per-protocol population.

End point type	Secondary

End point timeframe:

One month after second and third vaccination

End point values	rMenB	rMenB + OMV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	24		
Units: Percentage of subjects				
number (confidence interval 95%)				
Strain 44/76-SL - Post- 2nd Vaccination (N=25,23)	96 (80 to 100)	100 (85 to 100)		
Strain 44/76-SL - Post-3rd Vaccination	100 (86 to 100)	100 (86 to 100)		
Strain 5/99 - Post-2nd Vaccination (N=25,23)	100 (86 to 100)	100 (85 to 100)		
Strain 5/99 - Post-3rd Vaccination	100 (86 to 100)	100 (86 to 100)		
Strain NZ98/254 - Post-2nd Vaccination (N=24,22)	0 (0 to 14)	91 (71 to 99)		
Strain NZ98/254 - Post- 3rd Vaccination (N=22,24)	5 (0 to 23)	96 (79 to 100)		
Strain UKP1.7-2,4 - Post-2nd Vaccination (N=22,17)	0 (0 to 15)	88 (64 to 99)		
Strain UKP1.7-2,4 - Post-3rd Vaccination (N=20,20)	0 (0 to 17)	95 (75 to 100)		
Strain GB101 - Post-2nd Vaccination (N=21,18)	10 (1 to 30)	22 (6 to 48)		
Strain GB101 - Post-3rd Vaccination (N=21,19)	14 (3 to 36)	32 (13 to 57)		
Strain GB355 - Post-2nd Vaccination (N=5,7)	0 (0 to 52)	0 (0 to 41)		
Strain GB355 - Post-3rd Vaccination (N=7,6)	0 (0 to 41)	0 (0 to 46)		
Strain GB364 - Post-2nd Vaccination (N=17,14)	76 (50 to 93)	64 (35 to 87)		
Strain GB364 - Post-3rd Vaccination (N=15,15)	80 (52 to 96)	80 (52 to 96)		
287-953proteinantigen-Post-2ndVaccination(N=25,23)	100 (86 to 100)	100 (85 to 100)		
287-953proteinantigen-Post-3rdVaccination(N=24,25)	100 (86 to 100)	100 (86 to 100)		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Bactericidal Titers Against Meningococcal Strains One Month After Second and Third Vaccination of rMenB Vaccine With and Without OMV-NZ

End point title	Geometric Mean Bactericidal Titers Against Meningococcal Strains One Month After Second and Third Vaccination of rMenB Vaccine With and Without OMV-NZ

End point description:

The immune response was measured as the geometric mean bactericidal titers directed against meningococcal strains 44/76-SL, 5/99, NZ98/254, before vaccination (baseline) and one month after second vaccination (2 months after vaccination at 6-8 months) and third vaccination (at 12 months of age).
The analysis was performed on the per-protocol population.

End point type	Secondary

End point timeframe:

Baseline and one month after second and third vaccination

End point values	rMenB	rMenB + OMV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	24		
Units: Titers				
geometric mean (confidence interval 95%)				
Strain 44/76-SL - Baseline	1.16 (0.89 to 1.52)	1.7 (1.29 to 2.24)		
Strain 44/76-SL - Post- 2nd Vaccination (N=25,23)	94 (66 to 134)	250 (173 to 361)		
Strain 44/76-SL - Post-3rd Vaccination (N=24,24)	109 (79 to 153)	189 (136 to 263)		
Strain 5/99 - Baseline	1 (0.94 to 1.07)	1.05 (0.98 to 1.12)		
Strain 5/99 - Post-2nd Vaccination (N=25,23)	710 (532 to 947)	534 (395 to 721)		
Strain 5/99 - Post-3rd Vaccination (N=24,24)	1202 (929 to 1555)	906 (700 to 1172)		
Strain NZ98/254 - Baseline	1 (1 to 1)	1 (1 to 1)		
Strain NZ98/254 - Post- 2nd Vaccination (N=24,22)	1.06 (0.82 to 1.38)	27 (21 to 36)		
Strain NZ98/254 - Post- 3rd Vaccination (N=22,24)	1.21 (0.86 to 1.72)	44 (32 to 62)		
Strain UK P1.7-2,4 - Baseline (N=24,21)	1 (1 to 1)	1 (1 to 1)		
Strain UKP1.7-2,4 - Post- 2nd Vaccination (N=23,19	1 (0.75 to 1.34)	17 (12 to 24)		
Strain UKP1.7-2,4 - Post- 3rd Vaccination (N=21,22	1.07 (0.72 to 1.58)	34 (23 to 50)		
Strain GB101 - Baseline (N=24,21)	1.12 (0.81 to 1.56)	1.49 (1.05 to 2.11)		
Strain GB101 - Post-2nd Vaccination (N=22,21)	1.82 (1.14 to 2.9)	4.56 (2.83 to 7.35)		
Strain GB101 - Post-3rd Vaccination (N=22,22)	2.2 (1.14 to 4.23)	9.36 (4.87 to 18)		
Strain GB355 - Baseline (N=12,11)	1 (1 to 1)	1 (1 to 1)		
Strain GB355 - Post-2nd Vaccination (N=11,14)	1 (0.83 to 1.21)	1.16 (0.98 to 1.37)		
Strain GB355 – Post 3rd Vaccination (N=12,11)	1.06 (0.82 to 1.36)	1.46 (1.12 to 1.9)		

Strain GB364 - Baseline (N=22,17)	1.46 (1.19 to 1.79)	1.5 (1.19 to 1.9)		
Strain GB364 - Post-2nd Vaccination (N=19,16)	11 (6.39 to 19)	12 (6.75 to 23)		
Strain GB364 - Post-3rd Vaccination (N=17,19)	12 (6.17 to 22)	21 (11 to 37)		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean ELISA Concentration Against Meningococcal 287-953 Antigen One Month After Second and Third Vaccination of rMenB Vaccine With and Without OMV-NZ

End point title	Geometric Mean ELISA Concentration Against Meningococcal 287-953 Antigen One Month After Second and Third Vaccination of rMenB Vaccine With and Without OMV-NZ

End point description:

The immune response was measured as the geometric mean concentrations (GMCs) against the meningococcal antigen 287-953, evaluated using enzyme-linked immunosorbant assay (ELISA), before vaccination (baseline) and one month after second vaccination (2 months after vaccination at 6-8 months) and third vaccination (at 12 months of age).
The analysis was performed on the per-protocol population.

End point type	Secondary

End point timeframe:

Baseline and one month after second and third vaccination

End point values	rMenB	rMenB + OMV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	25		
Units: Titers				
geometric mean (confidence interval 95%)				
Antigen 287-953 - Baseline	24 (21 to 28)	21 (18 to 24)		
Antigen 287-953 - Post-2nd Vaccination (N=25,23)	1759 (1331 to 2324)	2912 (2178 to 3894)		
Antigen 287-953 - Post-3rd Vaccination (N=24,25)	2298 (1778 to 2970)	3521 (2739 to 4527)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Four-fold Rise in ELISA Concentration Against Meningococcal 287-953 Antigen One Month After Second and Third Vaccination of rMenB Vaccine With and Without OMV-NZ

End point title	Percentage of Subjects With Four-fold Rise in ELISA Concentration Against Meningococcal 287-953 Antigen One

	Month After Second and Third Vaccination of rMenB Vaccine With and Without OMV-NZ

End point description:

Immunogenicity was measured as the percentage of subjects who achieved a four-fold increase in ELISA geometric mean concentrations against meningococcal 287-953 antigen, one month after second vaccination (2 months after vaccination at 6-8 months) and third vaccination (at 12 months of age). The analysis was performed on the per-protocol population.

End point type	Secondary

End point timeframe:

One month after second and third vaccination

End point values	rMenB	rMenB + OMV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	25		
Units: Percentage of subjects				
number (confidence interval 95%)				
Antigen 287-953 - Post-2nd Vaccination (N=25,23)	100 (86 to 100)	100 (85 to 100)		
Antigen 287-953 - Post-3rd Vaccination (N=24,25)	100 (86 to 100)	100 (86 to 100)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Who Reported Solicited Local and Systemic Reactions After Each Vaccination of rMenB Vaccine With and Without OMV-NZ

End point title	Number of Subjects Who Reported Solicited Local and Systemic Reactions After Each Vaccination of rMenB Vaccine With and Without OMV-NZ

End point description:

Safety was assessed as the number of subjects who reported solicited local and systemic reactions from day 1 through day 7 after each vaccination of rMenB vaccine with and without OMV-NZ administered at 6-8 months (vaccination 1), 2 months later (vaccination 2) and at 12 months (vaccination 3). Analysis was done on safety set.

End point type	Secondary

End point timeframe:

Day 1 through day 7 after each vaccination

End point values	rMenB	rMenB + OMV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	30		
Units: Number of subjects				
Local reactions	29	29		
Tenderness - Vaccination 1	4	9		
Tenderness - Vaccination 2 (N=30,28)	5	11		

Tenderness - Vaccination 3 (N=30,27)	12	10		
Erythema - Vaccination 1	26	26		
Erythema - Vaccination 2 (N=30,28)	22	25		
Erythema - Vaccination 3 (N=30,27)	24	26		
Induration - Vaccination 1	15	18		
Induration - Vaccination 2 (N=30,28)	12	16		
Induration - Vaccination 3 (N=30,27)	15	18		
Swelling - Vaccination 1	4	11		
Swelling - Vaccination 2 (N=30,28)	9	10		
Swelling - Vaccination 3 (N=30,27)	11	9		
Systemic reactions	22	28		
Change in eating habits - Vaccination 1 (N=30,29)	6	8		
Change in eating habits - Vaccination 2 (N=30,27)	1	7		
Change in eating habits - Vaccination 3 (N=30,27)	8	5		
Sleepiness - Vaccination 1	7	11		
Sleepiness - Vaccination 2 (N=30,28)	7	8		
Sleepiness - Vaccination 3 (N=30,27)	7	4		
Vomiting - Vaccination 1	6	4		
Vomiting - Vaccination 2 (N=30,28)	1	3		
Vomiting - Vaccination 3 (N=30,27)	6	2		
Diarrhea - Vaccination 1	2	5		
Diarrhea - Vaccination 2 (N=30,28)	4	1		
Diarrhea - Vaccination 3 (N=30,27)	5	5		
Unusual crying - Vaccination 1	2	3		
Unusual crying - Vaccination 2 (N=30,28)	2	2		
Unusual crying - Vaccination 3 (N=30,27)	4	7		
Irritability - Vaccination 1	14	14		
Irritability - Vaccination 2 (N=30,28)	10	17		
Irritability - Vaccination 3 (N=30,28)	13	18		
Rash - Vaccination 1	3	3		
Rash - Vaccination 2 (N=30,28)	5	4		
Rash - Vaccination 3 (N=30,27)	5	4		
Fever (≥38 °C) - Vaccination 1	1	3		
Fever (≥38 °C) - Vaccination 2 (N=30,28)	2	3		
Fever (≥38 °C) - Vaccination 3 (N=30,27)	4	1		
Analg/Antipyr medications used - Vaccination 1	10	18		
Analg/Antipyr medications used - Vaccination 2	12	17		
Analg/Antipyr medications used - Vaccination 3	15	16		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Throughout the study period (day 1 to follow-up of 180 days after 12 months vaccination)	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups	
Reporting group title	rMenB + OMV
Reporting group description:	
6-8 month-old infants were administered 3 doses of Novartis rMenB with OMV-NZ vaccine at 6-8, 2 months later and at 12 months of age.	
Reporting group title	rMenB
Reporting group description:	
6-8 month-old infants were administered 3 doses of Novartis rMenB vaccine without OMV-NZ at 6-8, 2 months later and at 12 months of age.	

Serious adverse events	rMenB + OMV	rMenB	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 30 (3.33%)	5 / 30 (16.67%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Nervous system disorders			
Febrile convulsion			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Wheezing			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Croup infectious			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Localised infection			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	rMenB + OMV	rMenB	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	30 / 30 (100.00%)	30 / 30 (100.00%)	
Nervous system disorders			
Somnolence			
subjects affected / exposed	16 / 30 (53.33%)	14 / 30 (46.67%)	
occurrences (all)	27	27	
General disorders and administration site conditions			
Induration			
subjects affected / exposed	4 / 30 (13.33%)	1 / 30 (3.33%)	
occurrences (all)	4	2	
Injection site erythema			
subjects affected / exposed	28 / 30 (93.33%)	28 / 30 (93.33%)	
occurrences (all)	82	73	
Injection site induration			
subjects affected / exposed	26 / 30 (86.67%)	20 / 30 (66.67%)	
occurrences (all)	54	43	
Injection site swelling			
subjects affected / exposed	17 / 30 (56.67%)	14 / 30 (46.67%)	
occurrences (all)	30	26	

Pyrexia			
subjects affected / exposed	6 / 30 (20.00%)	7 / 30 (23.33%)	
occurrences (all)	7	10	
Swelling			
subjects affected / exposed	3 / 30 (10.00%)	0 / 30 (0.00%)	
occurrences (all)	5	0	
Crying			
subjects affected / exposed	10 / 30 (33.33%)	5 / 30 (16.67%)	
occurrences (all)	13	8	
Injection site pain			
subjects affected / exposed	18 / 30 (60.00%)	13 / 30 (43.33%)	
occurrences (all)	30	21	
Vaccination site erythema			
subjects affected / exposed	0 / 30 (0.00%)	2 / 30 (6.67%)	
occurrences (all)	0	2	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	10 / 30 (33.33%)	9 / 30 (30.00%)	
occurrences (all)	13	16	
Teething			
subjects affected / exposed	8 / 30 (26.67%)	8 / 30 (26.67%)	
occurrences (all)	13	11	
Vomiting			
subjects affected / exposed	7 / 30 (23.33%)	11 / 30 (36.67%)	
occurrences (all)	10	16	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	6 / 30 (20.00%)	3 / 30 (10.00%)	
occurrences (all)	6	3	
Rhinorrhoea			
subjects affected / exposed	1 / 30 (3.33%)	2 / 30 (6.67%)	
occurrences (all)	1	2	
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	2 / 30 (6.67%)	1 / 30 (3.33%)	
occurrences (all)	2	1	

Erythema			
subjects affected / exposed	4 / 30 (13.33%)	1 / 30 (3.33%)	
occurrences (all)	7	2	
Rash			
subjects affected / exposed	9 / 30 (30.00%)	8 / 30 (26.67%)	
occurrences (all)	16	19	
Psychiatric disorders			
Irritability			
subjects affected / exposed	25 / 30 (83.33%)	18 / 30 (60.00%)	
occurrences (all)	58	53	
Eating disorder			
subjects affected / exposed	14 / 30 (46.67%)	13 / 30 (43.33%)	
occurrences (all)	27	20	
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	5 / 30 (16.67%)	1 / 30 (3.33%)	
occurrences (all)	6	1	
Gastroenteritis			
subjects affected / exposed	4 / 30 (13.33%)	0 / 30 (0.00%)	
occurrences (all)	4	0	
Lower respiratory tract infection			
subjects affected / exposed	3 / 30 (10.00%)	2 / 30 (6.67%)	
occurrences (all)	3	2	
Nasopharyngitis			
subjects affected / exposed	3 / 30 (10.00%)	1 / 30 (3.33%)	
occurrences (all)	3	1	
Otitis media			
subjects affected / exposed	1 / 30 (3.33%)	2 / 30 (6.67%)	
occurrences (all)	1	2	
Rhinitis			
subjects affected / exposed	3 / 30 (10.00%)	5 / 30 (16.67%)	
occurrences (all)	4	5	
Tonsillitis			
subjects affected / exposed	2 / 30 (6.67%)	1 / 30 (3.33%)	
occurrences (all)	2	1	
Upper respiratory tract infection			

subjects affected / exposed	2 / 30 (6.67%)	0 / 30 (0.00%)	
occurrences (all)	3	0	
Varicella			
subjects affected / exposed	0 / 30 (0.00%)	2 / 30 (6.67%)	
occurrences (all)	0	2	
Viral rash			
subjects affected / exposed	2 / 30 (6.67%)	2 / 30 (6.67%)	
occurrences (all)	2	2	
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 30 (0.00%)	4 / 30 (13.33%)	
occurrences (all)	0	4	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 July 2008	The amendment was done to include the following: 1. An additional laboratory was included in the study where serology tests for this trial could be performed. 2. The laboratory related procedures for both laboratories involved in the study were drafted and aligned with the protocol accordingly. 3. Additionally, an immune response by ELISA testing was further explored for the subject's immune response in the trial and this was to demonstrate the possibility of performing additional future tests for future vaccine related projects according to subject's consent. 4. The sponsor's administrative structure, the cover page and the sponsor signature page were updated. 5. Blood draws were delayed for subjects taking antibiotics until 3 days after completion of antibiotic therapy. 6. Additional 30 minutes data on the Local & Systemic reaction page, was to be reported directly on the CRFs and are considered to be source data along with: demographics, medical history, pre-immunization axillary temperature, sites of immunizations. In addition to this, it was planned to categorize the measurements of body temperature as <38°C, 38-<39°C, 39-<40°C and ≥40°C, but was instead categorized as <38°C, 38-<38.5, 38.5-<39°C, 39-<39.5, 39.5-<40°C and ≥40°C. The root MSE from the PROC GLM output was used in the calculation of the 95% confidence intervals for each vaccine group associated with the geometric mean titers (GMTs) and geometric mean ratios (GMRs) for each visit and meningococcal strain, instead of the within group estimate of error at that visit, as specified in the AP.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/20844462