Clinical trial results:
A Phase 3, Randomized, Observer-blind, Multicenter Study to Evaluate the Immunogenicity and Safety of Novartis rMenB+OMV NZ Vaccine in Healthy Subjects Aged 11 to 17 years in Korea.

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

Summary

EudraCT number	2014-005083-15
Trial protocol	Outside EU/EEA
Global end of trial date	05 April 2014

Results information

Result version number	v2 (current)
This version publication date	04 June 2016
First version publication date	03 May 2015
Version creation reason	• Correction of full data set re-QC of study needed because of EudraCT system glitch and updates to results are required.

Trial information

Trial identification

Sponsor protocol code	V72_42

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01973218
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 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)	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	18 March 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	05 April 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Immunogenicity:
To assess the immunogenicity following two doses (Day 1 and Day 31) of Novartis rMenB+OMV NZ vaccine and control vaccines in healthy adolescents, as measured by the percentage of subjects with serum bactericidal activity (SBA) titer ≥ 1:4 against indicator strains H44/76, 5/99 and NZ98/254 one month after the second dose (Day 61).

Protection of trial subjects:

This clinical study was designed, implemented and reported in accordance with the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) Harmonized Tripartite Guidelines for Good Clinical Practice (GCP), with applicable local regulations, Novartis Vaccines and Diagnostics codes on protection of human rights, and with the ethical principles laid down in the Declaration of Helsinki (European Council 2001, US Code of Federal Regulations, ICH 1997).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 April 2014
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	Korea, Republic of: 264
Worldwide total number of subjects	264
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)	42
Adolescents (12-17 years)	222

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

Subject disposition

Recruitment

Recruitment details:

Subjects were recruited from 7 study centers in Korea.

Pre-assignment

Screening details:

All enrolled subjects 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	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	rMenB

Arm description:

Subjects received two doses of Meningococcal B Recombinant + Outer Membrane Vesicles New Zealand vaccine (rMenB+OMV NZ) vaccine (at Day 1 and Day 31) in the study.

Arm type	Experimental
Investigational medicinal product name	rMenB+ OMV NZ
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 0.5mL of rMenB+OMV NZ vaccine on Day 1 and Day 31.

Arm title	Placebo/MenACWY

Arm description:

Subjects received one dose of saline placebo (Day 1) and one dose of Meningococcal (groups A, C, W, and Y) Oligosaccharide Diphtheria CRM 197 Conjugate Vaccine (MenACWY-CRM) (Day 31) in the study.

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

Dosage and administration details:

Subjects received 0.5mL of MenACWY vaccine on Day 31 after receiving saline solution on Day 1.

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

Dosage and administration details:

Subjects received saline at Day 1.

Number of subjects in period 1	rMenB	Placebo/MenACWY
Started	176	88
Completed	174	88
Not completed	2	0
Consent withdrawn by subject	1	-
Adverse event	1	-

Baseline characteristics

Reporting groups	
Reporting group title	rMenB
Reporting group description:	
Subjects received two doses of Meningococcal B Recombinant + Outer Membrane Vesicles New Zealand vaccine (rMenB+OMV NZ) vaccine (at Day 1 and Day 31) in the study.	
Reporting group title	Placebo/MenACWY
Reporting group description:	
Subjects received one dose of saline placebo (Day 1) and one dose of Meningococcal (groups A, C, W, and Y) Oligosaccharide Diphtheria CRM 197 Conjugate Vaccine (MenACWY-CRM) (Day 31) in the study.	

Reporting group values	rMenB	Placebo/MenACWY	Total
Number of subjects	176	88	264
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	13.5	13.4	
standard deviation	± 1.8	± 1.8	-
Gender categorical Units: Subjects			
Female	77	36	113
Male	99	52	151

End points

End points reporting groups

Reporting group title	rMenB

Reporting group description:

Subjects received two doses of Meningococcal B Recombinant + Outer Membrane Vesicles New Zealand vaccine (rMenB+OMV NZ) vaccine (at Day 1 and Day 31) in the study.

Reporting group title	Placebo/MenACWY

Reporting group description:

Subjects received one dose of saline placebo (Day 1) and one dose of Meningococcal (groups A, C, W, and Y) Oligosaccharide Diphtheria CRM 197 Conjugate Vaccine (MenACWY-CRM) (Day 31) in the study.

Subject analysis set title	All Enrolled Set
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All subjects who have signed the informed consent, undergone screening procedures and were randomized.

Subject analysis set title	Safety Set (overall)
Subject analysis set type	Safety analysis

Subject analysis set description:

All subjects in the Exposed Set who have either post-vaccination adverse event or “reactogenicity” records. Subjects will be analyzed as "treated" (i.e., according to the vaccine a subject received, rather than the vaccine to which the subject may have been randomized).

Subject analysis set title	Full Analysis Set (FAS)
Subject analysis set type	Full analysis

Subject analysis set description:

All subjects in the Enrolled Population who received at least one dose of study vaccination and provide immunogenicity data at relevant time points.
FAS populations will be analyzed “as randomized” (i.e., subject is analyzed according to the vaccine he/she was designated to receive, which may be different from the vaccine the subject actually received).

Primary: 1. Percentage of subjects with human serum bactericidal antibody titers (SBA) ≥1:4 against Neisseria meningitidis serogroup B by vaccine group.

End point title	1. Percentage of subjects with human serum bactericidal antibody titers (SBA) ≥1:4 against Neisseria meningitidis serogroup B by vaccine group.[1]

End point description:

Percentage of subjects with SBA ≥1:4 against each of the three indicators strains of N.meningitidis serogroup B, at one month after second vaccination, were reported for each group.
Analysis was done on the Full Analysis Set i.e. all subjects who received at least one study vaccine and had immunogenicity data at relevant timepoints.

End point type	Primary

End point timeframe:

Day 1, Day 61

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 Endpoint.

End point values	rMenB	Placebo/MenACWY		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	174	88		
Units: Percentages of subjects				
number (confidence interval 95%)				
H44/76 strain (Day 1)	26 (20 to 33)	24 (15 to 34)		
H44/76 strain (Day 61)	98 (94 to 99)	27 (18 to 38)		
5/99 strain (Day 1)	12 (8 to 18)	10 (5 to 19)		
5/99 strain (Day 61)	97 (93 to 99)	16 (9 to 25)		
NZ98/254 strain (Day 1)	16 (10 to 22)	15 (8 to 24)		
NZ98/254 strain (Day 61)	97 (93 to 99)	17 (10 to 27)		

Statistical analyses

No statistical analyses for this end point

Secondary: 2. The SBA Geometric Mean Titers (GMTs) against N.meningitidis serogroup B, by vaccine group.

End point title	2. The SBA Geometric Mean Titers (GMTs) against N.meningitidis serogroup B, by vaccine group.

End point description:

The SBA antibody titers against each of the three indicator strains of N.meningitidis serogroup B at one month after second vaccination were reported as GMTs, for each group.
Analysis was done on the Full Analysis Set.

End point type	Secondary

End point timeframe:

Day 1, Day 61

End point values	rMenB	Placebo/MenACWY		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	174	88		
Units: Titers				
geometric mean (confidence interval 95%)				
H44/76 strain (Day 1)	2.31 (1.94 to 2.74)	2.18 (1.72 to 2.77)		
H44/76 strain (Day 61)	91 (74 to 112)	2.56 (1.91 to 3.43)		
5/99 strain (Day 1)	1.5 (1.31 to 1.72)	1.37 (1.16 to 1.61)		
5/99 strain (Day 61)	351 (284 to 432)	1.84 (1.34 to 2.52)		
NZ98/254 strain (Day 1)	1.71 (1.45 to 2.02)	1.59 (1.27 to 1.99)		
NZ98/254 strain (Day 61)	32 (26 to 40)	1.77 (1.35 to 2.32)		

Statistical analyses

No statistical analyses for this end point

Secondary: 3. The geometric mean ratio (GMRs) of post- versus pre-vaccination SBA titers Against N.meningitidis serogroup B, by vaccine group.

End point title	3. The geometric mean ratio (GMRs) of post- versus pre-vaccination SBA titers Against N.meningitidis serogroup B, by vaccine group.

End point description:

The GMRs of post-vaccination versus pre-vaccination SBA titers against each of the three indicator strains of N.meningitidis serogroup B, at one month after second vaccination (Day 61/Day 1) are reported, for each group.
Analysis was done on the Full Analysis Set.

End point type	Secondary

End point timeframe:

Day 61/ Day 1

End point values	rMenB	Placebo/MenACWY		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	174	88		
Units: Ratio				
geometric mean (confidence interval 95%)				
H44/76 strain	40 (32 to 49)	1.18 (0.92 to 1.51)		
5/99 strain	234 (181 to 301)	1.34 (1 to 1.81)		
NZ98/254 strain	19 (15 to 23)	1.11 (0.92 to 1.35)		

Statistical analyses

No statistical analyses for this end point

Secondary: 4. The percentages of subjects with a four-fold increase in SBA antibody titers against N.meningitidis serogroup B, by vaccine group.

End point title	4. The percentages of subjects with a four-fold increase in SBA antibody titers against N.meningitidis serogroup B, by vaccine group.

End point description:

Percentages of subjects with a four-fold increase in SBA antibody titers from baseline against each of the three indicator strains of N.meningitidis serogroup B, at one month after second vaccination are

reported, for each group.
Analysis was done on the Full Analysis Set.

End point type	Secondary

End point timeframe:

Day 61

End point values	rMenB	Placebo/MenACWY		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	174	88		
Units: Percentages of subjects				
number (confidence interval 95%)				
H44/76 strain	93 (88 to 96)	8 (3 to 16)		
5/99 strain	97 (93 to 99)	6 (2 to 13)		
NZ98/254 strain	83 (76 to 88)	6 (2 to 13)		

Statistical analyses

No statistical analyses for this end point

Secondary: 5. The Geometric mean concentrations (GMCs) against vaccine antigen 287-953, by vaccine group.

End point title	5. The Geometric mean concentrations (GMCs) against vaccine antigen 287-953, by vaccine group.

End point description:

The GMCs against vaccine antigen 287-953, at one month after second vaccination are reported, for each group.
Analysis was done on the Full Analysis Set.

End point type	Secondary

End point timeframe:

Day 1, Day 61

End point values	rMenB	Placebo/MenACWY		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	172	88		
Units: Concentrations IU/mL				
geometric mean (confidence interval 95%)				
Day 1	23 (22 to 24)	26 (23 to 29)		
Day 61	1208 (1025 to 1423)	27 (23 to 32)		

Statistical analyses

No statistical analyses for this end point

Secondary: 6. The GMR of post versus pre-vaccination GMCs against vaccine antigen 287-953, by vaccine group.

End point title	6. The GMR of post versus pre-vaccination GMCs against vaccine antigen 287-953, by vaccine group.

End point description:

The GMR of post-vaccination versus pre-vaccination GMCs against vaccine antigen 287-953, at one month after the second vaccination (Day 61/Day 1) are reported, for each group.
Analysis was done on the Full Analysis Set.

End point type	Secondary

End point timeframe:

Day 61/Day 1

End point values	rMenB	Placebo/MenACWY		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	172	88		
Units: Ratio				
geometric mean (confidence interval 95%)				
Day 61/Day 1	52 (44 to 62)	1.05 (0.9 to 1.22)		

Statistical analyses

No statistical analyses for this end point

Secondary: 7. The number of subjects reporting solicited adverse events (AEs) after each study vaccination, by vaccine group.

End point title	7. The number of subjects reporting solicited adverse events (AEs) after each study vaccination, by vaccine group.

End point description:

The number of subjects reporting solicited local and systemic AEs following vaccination rMenB+OMV NZ or placebo/MenACWY-CRM, are reported.
Analysis was done on the safety set for solicited AEs i.e all subjects who received the at least one study vaccination and had solicited AE data.

End point type	Secondary

End point timeframe:

Day 1 to Day 7 after each vaccination

End point values	rMenB	Placebo/MenACWY		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	174	88		
Units: Number of subjects				
Any Local (1st Vac; N=174,87)	160	22		
Inj. Site Pain (1st Vac; N=174,87)	158	18		
Inj. Site Erythema (1st Vac; TypeI; N=174,87)	62	5		
Inj. Site Eythema (1st Vac; TypeII; N=174,87)	14	0		
Inj. Site Swelling (1st Vac; TypeI; N=174,87)	57	0		
Inj. Site Swelling (1st Vac; TypeII; N=174,87)	19	0		
Inj. Site Induration (1st Vac; TypeI; N=174,87)	55	3		
Inj. Site Induration (1st Vac; TypeII; N=174,87)	29	0		
Any Local (2nd Vac; N=173,88)	145	36		
Inj. Site Pain (2nd Vac; N=173,88)	142	33		
Inj. Site Erythema (2nd Vac; TypeI; N=173,88)	49	17		
Inj. Site Erythema (2nd Vac; TypeII; N=173,88)	11	7		
Inj. Site Swelling (2nd Vac; TypeI; N=173,88)	47	16		
Inj. Site Swelling (2nd Vac; TypeII; N=173,88)	16	3		
Inj. Site Induration (2nd Vac; TypeI; N=173,88)	54	17		
Inj. Site Induration (2nd Vac; TypeII; N=173,88)	26	7		
Any Systemic (1st Vac; N=174,87)	89	31		
Loss of appetite (1st Vac; N=174,87)	15	8		
Nausea (1st Vac; N=174,87)	20	7		
Malaise (1st Vac; N=174,87)	51	13		
Myalgia (1st Vac; N=174,87)	45	10		
Arthralgia (1st Vac; N=174,87)	14	4		
Headache (1st Vac; N=174,87)	42	19		
Body Temp (≥38°C) (1st Vac; N=174,87)	6	1		
Prophy. use of Analg/Antipyr.(1st Vac; N=174,87)	1	0		
Therap. use of Analg/Antipyr.(1st Vac; N=174,87)	11	1		
Medically related Fever (1st Vac; N=174,86)	1	0		
Any Systemic (2nd Vac; N=173,88)	74	21		
Loss of appetite (2nd Vac; N=173,88)	21	4		
Nausea (2nd Vac; N=173,88)	15	5		
Malaise (2nd Vac; N=173,88)	47	10		
Myalgia (2nd Vac; N=173,88)	29	9		
Arthralgia (2nd Vac; N=173,88)	15	7		
Headache (2nd Vac; N=173,88)	50	16		
Body Temperature (≥38°C) (2nd Vac; N=173,88)	9	1		

Prophy use of Analg/Antipyr (2nd Vac) (N=173,88)	1	0		
Thera. use of Analg/Antipyr.(2nd Vac; N=173,88)	12	1		
Medically related Fever (2nd Vac; N=171,88)	2	0		

Statistical analyses

No statistical analyses for this end point

Secondary: 8. The number of subjects reporting unsolicited AEs after any vaccination, by vaccine group.

End point title	8. The number of subjects reporting unsolicited AEs after any vaccination, by vaccine group.

End point description:

The number of subjects reporting any unsolicited AEs, serious adverse events (SAEs), AEs leading to premature withdrawal and medically attended AEs (throughout the study), following vaccination rMenB+OMV NZ or placebo/MenACWY-CRM,were reported.

End point type	Secondary

End point timeframe:

Day 1 to Day 61

End point values	rMenB	Placebo/MenACWY		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	174	88		
Units: Number of subjects				
Any AEs	45	10		
Possibly or Probably Related AES	30	3		
SAEs	2	0		
At least possibly related SAEs	0	0		
Deaths	0	0		
Medically attended AEs	45	20		
AEs resulting in premature withdrawal	1	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Throughout the study	
Adverse event reporting additional description:	
Solicited AEs were collected between Day 1 to Day 7 after each vaccination; any unsolicited AEs (including serious AEs, medically attended AEs and AEs leading to premature withdrawal) from Day 1 to Day 61 (throughout the study).	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups	
Reporting group title	Placebo/MenACWY
Reporting group description:	
Subjects received one dose of saline placebo (Day 1) and one dose of MenACWY-CRM vaccine (Day 31) in the study.	
Reporting group title	rMenB
Reporting group description:	
Subjects received two doses of rMenB+OMV NZ vaccine (at Day 1 and Day 31) in the study.	

Serious adverse events	Placebo/MenACWY	rMenB	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 88 (0.00%)	2 / 175 (1.14%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Reproductive system and breast disorders			
Parovarian cyst			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 88 (0.00%)	1 / 175 (0.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Gastroenteritis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	0 / 88 (0.00%)	1 / 175 (0.57%)	
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	Placebo/MenACWY	rMenB	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	63 / 88 (71.59%)	167 / 175 (95.43%)	
Nervous system disorders			
Headache			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	31 / 88 (35.23%)	78 / 175 (44.57%)	
occurrences (all)	47	103	
General disorders and administration site conditions			
Injection Site Erythema			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	8 / 88 (9.09%)	25 / 175 (14.29%)	
occurrences (all)	9	28	
Injection Site Induration			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	7 / 88 (7.95%)	43 / 175 (24.57%)	
occurrences (all)	8	61	
Injection Site Pain			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	48 / 88 (54.55%)	166 / 175 (94.86%)	
occurrences (all)	63	322	
Malaise			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	17 / 88 (19.32%)	77 / 175 (44.00%)	
occurrences (all)	27	109	
Injection Site Swelling			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	4 / 88 (4.55%)	31 / 175 (17.71%)	
occurrences (all)	4	44	
Pyrexia			
alternative dictionary used: MedDRA 17.1			

subjects affected / exposed	2 / 88 (2.27%)	16 / 175 (9.14%)	
occurrences (all)	2	18	
Gastrointestinal disorders			
Nausea			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	10 / 88 (11.36%)	30 / 175 (17.14%)	
occurrences (all)	14	43	
Musculoskeletal and connective tissue disorders			
Arthralgia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	11 / 88 (12.50%)	26 / 175 (14.86%)	
occurrences (all)	15	33	
Myalgia			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	15 / 88 (17.05%)	60 / 175 (34.29%)	
occurrences (all)	21	81	
Infections and infestations			
Nasopharyngitis			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	14 / 88 (15.91%)	16 / 175 (9.14%)	
occurrences (all)	15	17	
Metabolism and nutrition disorders			
Decreased appetite			
alternative dictionary used: MedDRA 17.1			
subjects affected / exposed	11 / 88 (12.50%)	29 / 175 (16.57%)	
occurrences (all)	15	42	

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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

None

Notes: