Clinical trial results:
A Phase 3b, Single-Center, Open-label Study to Assess the Safety of Novartis Meningococcal B Recombinant Vaccine When Administered at a 0, 2-Month Schedule in Healthy at-risk Adults.

Summary

EudraCT number	2011-003694-29
Trial protocol	IT
Global end of trial date	13 November 2014

Results information

Result version number	v1 (current)
This version publication date	12 December 2016
First version publication date	15 May 2015

Trial information

Trial identification

Sponsor protocol code	V72_37

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01478347
WHO universal trial number (UTN)	-
Other trial identifiers	Sample data: Sample data

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma Services AG
Sponsor organisation address	Lichtstrasse 35, Basel, Switzerland, 4056
Public contact	Posting director, Novartis Pharma Services AG, RegistryContactVaccinesUS@novartis.com
Scientific contact	Posting director, Novartis Pharma Services AG, 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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	09 March 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	13 November 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To descriptively assess the safety of Novartis Recombinant Meningococcal B vaccine with Outer Membrane Vesicle from the New Zealand strain (rMenB+OMV NZ) in healthy at-risk adults when administered at a 0, 2-month schedule, throughout the clinical study.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 May 2013
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	Italy: 18
Worldwide total number of subjects	18
EEA total number of subjects	18

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)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	18
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were recruited from a single center (Siena, Italy).

Pre-assignment

Screening details:

All enrolled subjects participated in the study (n. 18 in part I and n. 12 subjects in part II of the study. However, in the safety set part II, n. 11 subjects were included since n. 1 was withdrawn after visit 3).

Period 1

Period 1 title	Visit 1 to Visit 7 (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	No
Arm title	Visit 1 to Visit 3

Arm description:

Healthy adults (≥18 to ≤65 years) at high risk for meningococcal B disease, due to routine occupational exposure to Neisseria meningitidis cultures (e.g. lab workers), were administered two injections of rMenB+OMV NZ vaccine, two months apart, in part I of 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:

The vaccine was administered by intramuscular (IM) injection into the deltoid region of the nondominant arm at a 0, 2-month vaccination schedule. The vaccine was supplied as a suspension for injection in a prefilled syringe (0.5 mL) containing 50 µg of each of the following 961c, 936-741, 287-953 N. Meningitidis purified antigens, 25 µg of OMV from N. meningitidis strain NZ 98/254, and 1.5 mg of aluminum hydroxide as adjuvant.

Arm title	Visit 4 to Visit 7

Arm description:

Healthy adults (≥18 to ≤65 years) at high risk for meningococcal B disease, due to routine occupational exposure to Neisseria meningitidis cultures (e.g. lab workers), who were administered two injections of rMenB+OMV NZ vaccine, two months apart, in part I of the study, were re-enrolled for optional blood draws and safety follow-up in part II of the study.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 1	Visit 1 to Visit 3	Visit 4 to Visit 7
Started	18	12
Completed	17	4
Not completed	1	8
Consent withdrawn by subject	-	4
Lost to follow-up	1	4

Baseline characteristics

Reporting groups	
Reporting group title	Visit 1 to Visit 7
Reporting group description:	
Healthy adults (≥18 to ≤65 years), at high risk for meningococcal B disease due to routine occupational exposure to N. meningitidis cultures (e.g. lab workers), who had received two injections of rMenB+OMV NZ vaccine in the part I of this study were re-enrolled for optional blood draws and safety follow-up in part II of the study.	

Reporting group values	Visit 1 to Visit 7	Total	
Number of subjects	18	18	
Age categorical Units: Subjects			

Age continuous			
Healthy adults (≥18 to ≤65 years), at high risk for meningococcal B disease due to routine occupational exposure to N. Meningitidis cultures (e.g. lab workers), were administered two injections of rMenB + OMV NZ vaccine, 2 months apart, in part I of the study.			
Units: years median standard deviation	 34.5 ± 5.7	 -	
Gender categorical			
Healthy adults (≥18 to ≤65 years), at high risk for meningococcal B disease due to routine occupational exposure to N. meningitidis cultures (e.g. lab workers), were administered two injections of rMenB + OMV NZ vaccine, 2 months apart, in part I of the study. In part II of the study subjects were re-enrolled for optional blood draws and safety follow-up.			
Units: Subjects			
Female	13	13	
Male	5	5	

End points

End points reporting groups

Reporting group title	Visit 1 to Visit 3

Reporting group description:

Healthy adults (≥18 to ≤65 years) at high risk for meningococcal B disease, due to routine occupational exposure to Neisseria meningitidis cultures (e.g. lab workers), were administered two injections of rMenB+OMV NZ vaccine, two months apart, in part I of the study.

Reporting group title	Visit 4 to Visit 7

Reporting group description:

Healthy adults (≥18 to ≤65 years) at high risk for meningococcal B disease, due to routine occupational exposure to Neisseria meningitidis cultures (e.g. lab workers), who were administered two injections of rMenB+OMV NZ vaccine, two months apart, in part I of the study, were re-enrolled for optional blood draws and safety follow-up in part II of the study.

Primary: 1. Number of subjects reporting unsolicited adverse events (AEs) following vaccination with two injections of rMenB+OMV NZ.

End point title	1. Number of subjects reporting unsolicited adverse events (AEs) following vaccination with two injections of rMenB+OMV NZ.[1][2]

End point description:

The number of subjects with serious adverse events (SAE), medically attended adverse events and AEs leading to premature withdrawal, following two injections of rMenB+OMV NZ vaccine are reported. This analysis was done on the safety set population i.e all subjects in the exposed set with unsolicited adverse event data for part I of the study.

End point type	Primary

End point timeframe:

Day 1 through Day 91.

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses were performed for this endpoint. All the analyses were run descriptively.
[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analyses were performed for this endpoint. All the analyses were run descriptively.

End point values	Visit 1 to Visit 3			
Subject group type	Reporting group			
Number of subjects analysed	18			
Units: Participants				
number (not applicable)				
Medically attended AEs	2			
At least possibly/probably related AEs	0			
SAEs	0			
At least possibly related SAEs	0			
Premature withdrawals due to AEs	0			

Statistical analyses

No statistical analyses for this end point

Primary: 2. Number of subjects reporting unsolicited AEs during Safety Follow-up (Part II of the Study).

End point title	2. Number of subjects reporting unsolicited AEs during Safety Follow-up (Part II of the Study).[3][4]

End point description:

The number of subjects (who were administered with two injections of rMenB+OMV NZ vaccine in the part I of this study) reporting unsolicited AEs during the safety follow-up in part II of the study, are reported. Unsolicited AEs in part II of the study include AEs considered to be related to blood draw procedure and all SAEs. This analysis was done on the safety set population i.e all subjects in the exposed set with unsolicited adverse event data for part II of the study.

End point type	Primary

End point timeframe:

Day 151 to day 331. Subject's eligibility for participation in part II of this trial was confirmed starting from day 92 on. Next study visit (visit 4, day 151) was scheduled upon subject's agreement to continue in the trial.

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: No statistical analyses were performed for this endpoint. All the analyses were run descriptively.
[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analyses were performed for this endpoint. All the analyses were run descriptively.

End point values	Visit 4 to Visit 7			
Subject group type	Reporting group			
Number of subjects analysed	11[5]			
Units: Participants				
number (not applicable)				
All AEs	0			
SAEs	0			
At least possibly related SAEs	0			

Notes:

[5] - Of the 12 subjects enrolled for part II, one was withdrawn after Visit 3 (reason: lost to follow-up)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All serious AEs and other unsolicited AEs collected from Day 1 to Day 331 (throughout the study) for subjects who participated in both part I and II of the study, are reported.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	Visit 1 to Visit 7

Reporting group description:

Healthy adults (≥18 to ≤65 years), at high risk for meningococcal B disease due to routine occupational exposure to N. meningitidis cultures (e.g. lab workers), were administered two injections of rMenB + OMV NZ vaccine, 2 months apart, in part I of the study. In part II of the study subjects were re-enrolled for optional blood draws and safety follow-up.

Serious adverse events	Visit 1 to Visit 7		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 18 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Visit 1 to Visit 7		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 18 (11.11%)		
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Pharyngitis			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 November 2012	The amendment included the following changes: - The trial was to be conducted in a single country. - The maximum age for enrollment was extended to ≤ 65 years from ≤ 60 years in the original protocol. - To specify the eligibility for enrollment of Novartis' employees. - The 'at-risk' subjects to be enrolled into this trial also included travelers to MenB epidemic area in the original protocol. According to the first amendment the travelers to these areas were not to be enrolled. - The first protocol amendment also extended the study (to part II) to include additional blood draws from high responders to the study vaccine.
14 December 2012	It included changes to the study entry criteria: - a subject could continue to participate in part II of the protocol if he had hematocrit value higher than 32% for female subjects or higher than 35% for male subjects. In the original protocol these were specified as hemoglobin not lower than 12.5 g/dL for females and 13.5 g/dL for males. - For female subjects if sexually active, they were to use one of the accepted birth control methods at least 1 month prior to study entry rather than 2 months prior to study entry as mentioned in the original protocol.
17 September 2013	Information on marketing authorization was updated and duration of safety data collection period was clarified.
29 January 2014	It was specified that a urine pregnancy test had to be obtained only from female subjects of child bearing potential. Written informed consent was explicitly required as part of the inclusion criteria in protocol part II.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported