Clinical trial results:
A Phase 2b, Randomized, Controlled, Observer-Blind, Multi-Center Study Assessing the Effectiveness, Immunogenicity and Safety of Novartis Meningococcal ABCWY Vaccine Administered to Healthy Adolescents in the U.S.

Summary

EudraCT number	2015-000979-27
Trial protocol	Outside EU/EEA
Global end of trial date	16 February 2015

Results information

Result version number	v1 (current)
This version publication date	27 February 2016
First version publication date	27 February 2016

Trial information

Trial identification

Sponsor protocol code	V102_16

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02140762
WHO universal trial number (UTN)	-

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	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	04 February 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	16 February 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the effectiveness of the MenABCWY vaccine against a randomly selected panel of endemic US Neisseria meningitidis (N. meningitidis) serogroup B invasive disease strains as measured by bactericidal activity at 1:4 dilution using endogenous complement human Serum Bactericidal Assay (enc-hSBA) at one month after the two vaccinations, when compared to a single dose of MenACWY.

Protection of trial subjects:

This clinical study was designed and shall be implemented and reported in accordance with the International Counsil for Harmonisation (ICH) Harmonized Tripartite Guidelines for Good Clinical Practice, 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, Novartis 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).
Eligible subjects may only be included in the study after providing written informed Consent.

Background therapy: -

Evidence for comparator:

MenACWY was used as active-comparator to evaluate the effectiveness of MenABCWY.

Actual start date of recruitment	29 May 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	United States: 305
Worldwide total number of subjects	305
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)	182

Adolescents (12-17 years)	109
Adults (18-64 years)	14
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were recruited from 8 study sites in USA.

Pre-assignment

Screening details:

All enrolled subjects were included in the trial.

Period 1

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

Blinding implementation details:

Observer blind

Arms

Are arms mutually exclusive?	Yes
Arm title	MenABCWY

Arm description:

Subjects received one dose of MenABCWY vaccine at visit day 1 and a second dose at visit month 2.

Arm type	Experimental
Investigational medicinal product name	MenABCWY
Investigational medicinal product code	
Other name	MenACWY conjugate combined with rMenB + OMV
Pharmaceutical forms	Powder for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL dose in the deltoid area of the non dominant arm.

Arm title	Placebo/MenACWY

Arm description:

Subjects received one dose of placebo at visit day 1 and one dose of MenACWY vaccine at visit month 2.

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

Dosage and administration details:

0.5 mL dose in the deltoid area of non dominant arm.

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

Dosage and administration details:

0.5 mL saline solution in the deltoid area of non dominant arm.

Number of subjects in period 1	MenABCWY	Placebo/MenACWY
Started	154	151
Completed	137	139
Not completed	17	12
Consent withdrawn by subject	6	4
Other	-	1
Adverse event	1	1
Lost to follow-up	9	5
Protocol deviation	1	1

Baseline characteristics

Reporting groups	
Reporting group title	MenABCWY
Reporting group description:	
Subjects received one dose of MenABCWY vaccine at visit day 1 and a second dose at visit month 2.	
Reporting group title	Placebo/MenACWY
Reporting group description:	
Subjects received one dose of placebo at visit day 1 and one dose of MenACWY vaccine at visit month 2.	

Reporting group values	MenABCWY	Placebo/MenACWY	Total
Number of subjects	154	151	305
Age categorical Units: Subjects			
Children (2-11 years)	94	88	182
Adolescents (12-17 years)	54	55	109
Adults (18-64 years)	6	8	14
Age continuous Units: years			
arithmetic mean	11.9	12.2	
standard deviation	± 2.18	± 2.42	-
Gender categorical Units: Subjects			
Female	67	61	128
Male	87	90	177

End points

End points reporting groups

Reporting group title	MenABCWY
Reporting group description:	
Subjects received one dose of MenABCWY vaccine at visit day 1 and a second dose at visit month 2.	
Reporting group title	Placebo/MenACWY
Reporting group description:	
Subjects received one dose of placebo at visit day 1 and one dose of MenACWY vaccine at visit month 2.	
Subject analysis set title	All enrolled set
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All screened subjects who provided informed consent and received a subject ID, regardless of the subject’s randomization and treatment status in the trial.	
Subject analysis set title	Exposed Set
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All subjects in the All Enrolled Set who received a study vaccination.	
Subject analysis set title	Full Analysis Set (FAS) effectiveness (month 3)
Subject analysis set type	Full analysis
Subject analysis set description:	
All subjects in the All Enrolled Set who: received a study vaccination and provided evaluable serum sample with enc-hSBA for at least one N. meningitidis serogroup B invasive disease strain at one month after the 2-dose series (Visit Month 3).	

Subject analysis set title	Full Analysis Set (FAS) immunogenicity (month 3)
Subject analysis set type	Full analysis
Subject analysis set description:	
All subjects in the All Enrolled Set who received a study vaccination and provided evaluable serum samples respectively at one month post-second vaccination (Visit Month 3) whose immunogenicity assay result is available for at least one N. meningitidis serogroup B test strain or serogroups A, C, W or Y.	
Subject analysis set title	Solicited Safety Set
Subject analysis set type	Safety analysis
Subject analysis set description:	
All subjects in the All Exposed Set who have provided any solicited adverse event data and/or other indicators or reactogenicity.	
Subject analysis set title	Unsolicited Safety Set
Subject analysis set type	Safety analysis
Subject analysis set description:	
All subjects in the All Exposed Set who have post-vaccination unsolicited adverse event records.	
Subject analysis set title	Overall Safety Set
Subject analysis set type	Safety analysis
Subject analysis set description:	
All subjects in the All Exposed Set who have either post-vaccination unsolicited adverse event or reactogenicity records.	

Primary: Percentage of subjects without bactericidal activity at 1:4 dilution against each US Neisseria meningitidis (N. meningitidis) serogroup B strain at one month after the second injection

End point title	Percentage of subjects without bactericidal activity at 1:4 dilution against each US Neisseria meningitidis (N. meningitidis) serogroup B strain at one month after the second injection

End point description:

The combined percentage of subjects without bactericidal activity at 1:4 dilution using the endogenous complement human Serum Bactericidal Assay (enc-hSBA) across all strains in MenABCWY group and MenACWY group is reported at one month after the second injection. The percentage of subjects without bactericidal activity at 1:4 dilution was used to assess the effectiveness of two doses of MenABCWY vaccine when compared to one dose of MenACWY vaccine against a panel of US N. meningitidis serogroup B invasive disease strains. Least Square (LS)-mean computed from the generalised linear model.
Analysis was done on FAS effectiveness (month 3).

End point type	Primary

End point timeframe:

One month after the second vaccination (month 3)

End point values	MenABCWY	Placebo/MenACWY		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	139	135		
Units: Percentages of subjects				
arithmetic mean (standard deviation)	25.17 (± 30.77)	76.19 (± 27.32)		

Statistical analyses

Statistical analysis title	Combined Serogroup B Strains Vaccine Effectiveness

Statistical analysis description:

H0 (Null Hypothesis): Vaccine Effectiveness (VE) ≤10%.
If the lower limit of 95% CI for VE is > 10% the null hypothesis is to be rejected and effectiveness declared. The VE at 1 month after the 2nd injection for each strain is defined as [1 - (% of subjects without bactericidal activity at 1:4 dilution in MenABCWY group / % of subjects without bactericidal activity at 1:4 dilution in MenACWY group)] x 100. The combined VE across all strains was computed by mean of a generalized linear model.

Comparison groups	Placebo/MenACWY v MenABCWY
Number of subjects included in analysis	274
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	< 0.0001
Method	Generalized Linear Model
Parameter estimate	Vaccine Effectiveness
Point estimate	67
Confidence interval	
level	95 %
sides	2-sided
lower limit	65
upper limit	69

Notes:

[1] - VE is based on the relative risk (RR). The Poisson Distibution and Log Link options were used in the generalized linear model to compute the log10 RR and the corresponding confidence interval. Fixed effects:treatment group, strain (and center).

Secondary: Percentages of Subjects Without Bactericidal Activity at 1:8 dilution against each US N. meningitidis serogroup B strain at one month after the second injection

End point title	Percentages of Subjects Without Bactericidal Activity at 1:8 dilution against each US N. meningitidis serogroup B strain at one month after the second injection

End point description:

The combined percentage of subjects without bactericidal activity at 1:8 dilution using the endogenous complement human Serum Bactericidal Assay (enc-hSBA) across all strains in MenABCWY group and MenACWY group is reported at one month after the second injection. The percentage of subjects without bactericidal activity at 1:8 dilution was used to assess the effectiveness of two doses of MenABCWY vaccine when compared to one dose of Men ACWY vaccine against a panel of US N. meningitidis serogroup B invasive disease strains. Least Square (LS)-mean computed from the generalized linear model.
Analysis was done on FAS effectiveness (month 3).

End point type	Secondary

End point timeframe:

One month after the second vaccination (month 3)

End point values	MenABCWY	Placebo/MenACWY		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	139	135		
Units: Percentages of subjects				
arithmetic mean (standard deviation)	47.7 (± 37.04)	88.28 (± 22.05)		

Statistical analyses

Statistical analysis title	Combined Serogroup B Strains Vaccine Effectiveness

Statistical analysis description:

H0 (Null Hypothesis): Vaccine Effectiveness (VE) ≤10%.
If the lower limit of the 95% CI for VE is > 10% the null hypothesis is to be rejected and effectiveness declared. The VE at 1 month after the second injection for each strain is defined as [1 -(% of subjects without bactericidal activity at 1:8 dilution in MenABCWY group/% of subjects without bactericidal activity at 1:8 dilution in MenACWY group)]x100. The combined VE across all strains was computed by mean of a generalized linear model.

Comparison groups	MenABCWY v Placebo/MenACWY
Number of subjects included in analysis	274
Analysis specification	Pre-specified
Analysis type	superiority[2]
P-value	< 0.0001
Method	Generalized Linear Model
Parameter estimate	Vaccine Effectiveness
Point estimate	46
Confidence interval	
level	95 %
sides	2-sided
lower limit	43
upper limit	49

Notes:

[2] - VE is based on the relative risk (RR). The Poisson Distribution and Log Link options were used in the generalized linear model to compute the log10 RR and the corresponding confidence interval. Fixed effects:treatment group, strain (and center).

Secondary: Percentages of strains with Vaccine Effectiveness (VE) values corresponding to predefined ranges at 1:4 dilution at one month after the second vaccination

End point title	Percentages of strains with Vaccine Effectiveness (VE) values corresponding to predefined ranges at 1:4 dilution at one month after the second vaccination[3]

End point description:

Percentages of strains with VE values from 0% through <10%, from 10% through < 30%, from 30% through < 60%, from 60% through 100% at 1:4 dilution at one month after the second vaccination against each of the endemic US N. meningitidis serogroup B strains. Each individual strain data was analysed separately with treatment group as only independent variable in the model.
The effectiveness of two doses of MenABCWY vaccine was compared to one dose of Men ACWY vaccine. Analysis was done on FAS effectiveness (month 3).

End point type	Secondary

End point timeframe:

One month after the second vaccination (month 3).

Notes:

[3] - 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 analysis was aassociated to this endpoint.

End point values	MenABCWY			
Subject group type	Reporting group			
Number of subjects analysed	110[4]			
Units: Percentages of strains				
number (not applicable)				
VE=0% through <10%	4.6			
VE=0% through <10% (Min)	0			
VE=0% through <10% (Max)	8			
VE=10% through <30%	12.7			
VE=10% through <30% (Min)	13			
VE=10% through <30% (Max)	29			
VE=30% through <60%	18.2			
VE=30% through <60% (Min)	31			
VE=30% through <60% (Max)	60			
VE=60% through 100%	59.1			
VE=60% through 100% (Min)	61			
VE=60% through 100% (Max)	99			

Notes:

[4] - Number of strains tested for VE per study group

Statistical analyses

No statistical analyses for this end point

Secondary: Percentages of strains with VE values corresponding to predefined ranges at 1:8 dilution at one month after the second vaccination

End point title	Percentages of strains with VE values corresponding to predefined ranges at 1:8 dilution at one month after the second vaccination[5]

End point description:

Percentages of strains with VE values from 0% through <10%, from 10% through <30%, from 30% through <60%, 60% through 100% at 1:8 dilution at one month after the second vaccination against each of the endemic US N. meningitidis serogroup B strains. Each individual strain data was analysed separately with treatment group as only independent variable in the model. The effectiveness of two

doses of MenABCWY vaccine was compared to one dose of Men ACWY vaccine.
Analysis was done on FAS effectiveness (Month 3).

End point type	Secondary

End point timeframe:

One month after the second vaccination (month 3)

Notes:

[5] - 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 analysis was aassociated to this endpoint.

End point values	MenABCWY			
Subject group type	Reporting group			
Number of subjects analysed	110[6]			
Units: Percentages of strains				
number (not applicable)				
VE=0% through <10%	25.5			
VE=0% through <10% (Min)	0			
VE=0% through <10% (Max)	10			
VE=10% through <30%	19.1			
VE=10% through <30% (Min)	10			
VE=10% through <30% (Max)	27			
VE=30% through <60%	10.9			
VE=30% through <60% (Min)	32			
VE=30% through <60% (Max)	56			
VE=60% through 100%	40.9			
VE=60% through 100% (Min)	62			
VE=60% through 100% (Max)	99			

Notes:

[6] - Number of strains tested for VE per study group

Statistical analyses

No statistical analyses for this end point

Secondary: Percentages of N. meningitidis serogroup B invasive disease strains killed at 1:4 and 1:8 dilutions, for each subject

End point title	Percentages of N. meningitidis serogroup B invasive disease strains killed at 1:4 and 1:8 dilutions, for each subject

End point description:

The mean percentage of N. meningitidis serogroup B invasive disease strains killed by each subject, at 1:4 and 1:8 dilutions at one month after the 2-dose vaccination series is reported.
Analysis was done on FAS effectiveness (month 3).

End point type	Secondary

End point timeframe:

Baseline, one month after second vaccination (month 3)

End point values	MenABCWY	Placebo/MenACWY		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	139	135		
Units: Mean percentage of strains				
arithmetic mean (standard deviation)				
Baseline (1:4) (N=136, 132)	20.08 (± 16.25)	19.76 (± 15.48)		
1 month after 2nd vaccination (1:4)	74.47 (± 14.55)	22.93 (± 16.11)		
Baseline (1:8) (N=136, 132)	9.25 (± 8.35)	9.54 (± 9.49)		
1 month after 2nd vaccination (1:8)	52.16 (± 17.11)	11.39 (± 10.35)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentages of subjects with enc-hSBA titer ≥ 1:4 and enc-hSBA titer ≥ 1:8 at one month after the 2-dose vaccination series

End point title	Percentages of subjects with enc-hSBA titer ≥ 1:4 and enc-hSBA titer ≥ 1:8 at one month after the 2-dose vaccination series

End point description:

The immunogenicity of two doses of MenABCWY vaccine compared to a single dose of MenACWY vaccine, in terms of percentages of subjects with enc-hSBA ≥ 1:4 and enc-hSBA titer ≥ 1:8 against four N. meningitidis serogroup B test strains at one month after the 2-dose vaccination series is reported. Analysis was done on the FAS immunogenicity (month 3).

End point type	Secondary

End point timeframe:

One month after the second vaccination (month 3)

End point values	MenABCWY	Placebo/MenACWY		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	134	130		
Units: Percentage of subjects				
number (confidence interval 95%)				
NZ98/254 (1:4, 1 month after 2nd vacc) (N=132,130)	67 (57.9 to 74.6)	1 (0.02 to 4.2)		
NZ98/254 (1:8, 1 month after 2nd vacc) (N=132,130)	24 (17.2 to 32.5)	0 (0 to 2.8)		
M14459 (1:4, 1 month after 2nd vacc) (N=134,129)	96 (90.5 to 98.3)	12 (7.3 to 19.4)		
M14459 (1:8, 1 month after 2nd vacc) (N=134,129)	64 (55.4 to 72.3)	3 (0.9 to 7.7)		
M07-0241084(1:4,1 month after 2nd vacc)(N=131,120)	59 (49.8 to 67.3)	20 (13.3 to 28.3)		
M07-0241084(1:8,1 month after 2nd vacc)(N=131,120)	21 (14.7 to 29.4)	7 (2.9 to 12.7)		
96217 (1:4, 1 month after 2nd vacc) (N=93,82)	100 (96.1 to 100)	49 (37.6 to 60.1)		

96217 (1:8, 1 month after 2nd vacc) (N=93,82)	99 (94.2 to 99.97)	15 (7.8 to 24.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: hSBA Geometric Mean Titers (GMTs) against the N. meningitidis serogroup B test strains

End point title	hSBA Geometric Mean Titers (GMTs) against the N. meningitidis serogroup B test strains

End point description:

The immunogenicity of two doses of MenABCWY compared to a single dose of MenACWY vaccine, in terms of hSBA GMTs against serogroup B test strains, at one month after the 2-dose vaccination series. Analysis was done on the FAS immunogenicity (month 3).

End point type	Secondary

End point timeframe:

One month after the second vaccination (month 3)

End point values	MenABCWY	Placebo/MenACWY		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	138	133		
Units: Titers				
geometric mean (confidence interval 95%)				
NZ98/254 (1 month after 2nd vacc)	6.03 (5.16 to 7.03)	1.04 (0.89 to 1.22)		
M14459 (1 month after 2nd vacc) (N=138,132)	13.4 (11 to 16)	1.08 (0.92 to 1.28)		
M07-0241084 (1 month after 2nd vacc)(N=124,122)	5.05 (4.08 to 6.26)	1.65 (1.33 to 2.05)		
96217 (1 month after 2nd vacc) (N=124,118)	169.22 (133 to 215)	3.16 (2.48 to 4.04)		

Statistical analyses

No statistical analyses for this end point

Secondary: hSBA Geometric Mean Titers (GMTs) Against the N. Meningitidis Serogroups A,C,W,Y

End point title	hSBA Geometric Mean Titers (GMTs) Against the N. Meningitidis Serogroups A,C,W,Y

End point description:

The immunogenicity of two doses of MenABCWY compared to a single dose of MenACWY vaccine, in terms of hSBA GMTs to serogroups A, C, W, and Y, at one month after the 2-dose vaccination series. Analysis was done on FAS Immunogenicity (Month 3).

End point type	Secondary

End point timeframe:

One month after the second vaccination (month 3)

End point values	MenABCWY	Placebo/MenACWY		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	137	125		
Units: Titers				
geometric mean (confidence interval 95%)				
Men C (1 month after 2nd vacc) (N=134,125)	235.88 (171 to 325)	38.61 (28 to 54)		
Men W (1 month after 2nd vacc) (N=119,115)	157.72 (120 to 207)	37.51 (28 to 49)		
Men Y (1 month after 2nd vacc) (N=107,94)	154.43 (110 to 220)	27.76 (19 to 40)		
Men A (1 month after 2nd vacc) (N=137,115)	77.02 (59 to 101)	22.08 (17 to 30)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Reporting Solicited Local and Systemic Adverse Events (AEs)

End point title	Number of Subjects Reporting Solicited Local and Systemic Adverse Events (AEs)

End point description:

Reactogenicity was presented in terms of number of subjects reporting solicited local and systemic AEs and other indicators.
Analysis was done on Solicited Safety Set.

End point type	Secondary

End point timeframe:

From day 1 (6 hours) until day 7 after any vaccination

End point values	MenABCWY	Placebo/MenACWY		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	149	146		
Units: Number of subjects				
Any	129	92		
Any Local Reactions	128	65		
Any Systemic Reactions	70	66		
Induration (mm) (N=149,145)	21	8		
Erythema (mm) (N=149,145)	23	5		
Pain (N=149,145)	127	63		

Nausea	9	19		
Fatigue	40	35		
Myalgia	20	14		
Arthralgia	18	5		
Headache	40	42		
Fever (N=148,146)	9	0		
Chills	15	8		
Loss of appetite	23	12		
Prevention of pain/fever (N=149,144)	4	2		
Treatment of pain/fever (N=149,144)	60	9		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentages of subjects reporting unsolicited AEs

End point title	Percentages of subjects reporting unsolicited AEs

End point description:

Percentages of subjects reporting unsolicited AEs including serious adverse events (SAEs).
Analysis was done on the unsolicited safety set. Analysis for AEs leading to withdrawal was done on All Enrolled Set population.

End point type	Secondary

End point timeframe:

From day 1 to day 30 after any vaccination for any unsolicited AE. From day 1 to study termination (day 181) for all other categories.

End point values	MenABCWY	Placebo/MenACWY		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	150	146		
Units: Percentages of subjects				
Any unsolicited AEs	19	19		
Possibly or probably related AEs	5	2		
Medically-attended AEs	25	30		
AEs leading to withdrawal (N=154, 151)	1	1		
Any SAEs	0	1		
SAE leading to death	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited adverse events (AEs): from Day 1 to Day 7 of each study vaccination. Unsolicited AEs from Day 1 to Day 30 after each vaccination. Serious AEs, medically attended AEs, AEs leading to withdrawal were collected for the whole duration of the study.

Adverse event reporting additional description:

Data are presented in terms of number of subjects reporting AEs. Data are presented in terms of number of subjects reporting AEs with a frequency > 5% in at least one group.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups

Reporting group title	Placebo/MenACWY

Reporting group description:

Subjects received one dose of placebo at day 1 and one dose of MenACWY vaccine after 2 months

Reporting group title	MenABCWY

Reporting group description:

Subjects received one dose of MenABCWY vaccine at day 1 and a second dose after 2 months

Serious adverse events	Placebo/MenACWY	MenABCWY	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 149 (0.67%)	0 / 152 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Infections and infestations			
Pharyngitis			
subjects affected / exposed[1]	1 / 146 (0.68%)	0 / 150 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Not all subjects in the Exposed Population provided safety information.

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

Non-serious adverse events	Placebo/MenACWY	MenABCWY	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	100 / 149 (67.11%)	132 / 152 (86.84%)	
Nervous system disorders			

Headache			
alternative assessment type: Systematic			
subjects affected / exposed[2]	44 / 147 (29.93%)	42 / 151 (27.81%)	
occurrences (all)	128	100	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed[3]	40 / 147 (27.21%)	42 / 151 (27.81%)	
occurrences (all)	81	105	
Chills			
subjects affected / exposed[4]	9 / 147 (6.12%)	15 / 151 (9.93%)	
occurrences (all)	15	31	
Injection site erythema			
alternative assessment type: Systematic			
subjects affected / exposed[5]	24 / 147 (16.33%)	60 / 151 (39.74%)	
occurrences (all)	48	171	
Injection site induration			
alternative assessment type: Systematic			
subjects affected / exposed[6]	16 / 147 (10.88%)	51 / 151 (33.77%)	
occurrences (all)	50	173	
Injection site pain			
alternative assessment type: Systematic			
subjects affected / exposed[7]	71 / 147 (48.30%)	130 / 151 (86.09%)	
occurrences (all)	152	575	
Pyrexia			
alternative assessment type: Systematic			
subjects affected / exposed[8]	0 / 147 (0.00%)	11 / 151 (7.28%)	
occurrences (all)	0	15	
Gastrointestinal disorders			
Nausea			
alternative assessment type: Systematic			
subjects affected / exposed[9]	20 / 147 (13.61%)	10 / 151 (6.62%)	
occurrences (all)	46	22	
Musculoskeletal and connective tissue disorders			

Arthralgia			
alternative assessment type: Systematic			
subjects affected / exposed[10]	7 / 147 (4.76%)	19 / 151 (12.58%)	
occurrences (all)	10	41	
Myalgia			
alternative assessment type: Systematic			
subjects affected / exposed[11]	15 / 147 (10.20%)	23 / 151 (15.23%)	
occurrences (all)	27	39	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed[12]	12 / 147 (8.16%)	24 / 151 (15.89%)	
occurrences (all)	31	54	

Notes:

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Not all subjects in the Exposed Population provided safety information.

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Not all subjects in the Exposed Population provided safety information.

[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Not all subjects in the Exposed Population provided safety information.

[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Not all subjects in the Exposed Population provided safety information.

[6] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Not all subjects in the Exposed Population provided safety information.

[7] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Not all subjects in the Exposed Population provided safety information.

[8] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Not all subjects in the Exposed Population provided safety information.

[9] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Not all subjects in the Exposed Population provided safety information.

[10] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Not all subjects in the Exposed Population provided safety information.

[11] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Not all subjects in the Exposed Population provided safety information.

[12] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Not all subjects in the Exposed Population provided safety information.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 March 2014	The protocol has been amended: to reflect the revised plan to restrict access to subject group assignments for both of the planned final analyses and to generate individual data listings with subject group assignments only after full unblinding of the extension study (V102_16E1); to clarify elements of the Interactive Response Technology randomization procedures; to address the new End of Study definition in compliance with the Novartis Quality Manual and the Corporate Data Disclosure Policy.
03 February 2015	The protocol has been amended: to replace the NadA M01-0240364 strain with NadA strain 96217, in accordance to per Center for Biologics Evaluation and Research Office of Vaccines Research and Review (CBER) feedback on HT-hSBA validation plan; to clarify that subjects should not have reportable protocol deviations leading to exclusion for period prior to Visit Month 3/Visit Month 6 (except for blood draws and serological results missing); to revised definition and evaluation of protocol deviations, according to changes made to the Novartis Vaccines internal process of defining and evaluating protocol deviations.

Notes:

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: