Clinical trial results:
A Phase 3, Multicenter, Open-label Study to Evaluate Immunogenicity and Safety of Novartis Meningococcal ACWY Conjugate Vaccine (MenACWY-CRM) in Healthy Subjects From 2 to 18 Years in Taiwan.

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

Summary

EudraCT number	2014-004973-17
Trial protocol	Outside EU/EEA
Global end of trial date	21 January 2012

Results information

Result version number	v2 (current)
This version publication date	01 June 2016
First version publication date	15 March 2015
Version creation reason	• Correction of full data set re-QC study because of EudraCT system glitch and updates to results are required.

Trial information

Trial identification

Sponsor protocol code	V59_49

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01410474
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Vaccines and Diagnostics S.r.l
Sponsor organisation address	Via Fiorentina 1, Siena, Italy, 53100
Public contact	Posting Director, Novartis Vaccines , RegistryContactVaccinesUS@novartis.com
Scientific contact	Posting Director, Novartis Vaccines , RegistryContactVaccinesUS@novartis.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	21 January 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	21 January 2012
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the immunogenicity of a single injection of MenACWY-CRM as measured by the percentage of subjects with Human Serum Bactericidal Assay (hSBA) seroresponse, directed against N meningitidis serogroups A, C, W135 and Y.

Protection of trial subjects:

This trial was performed with the ethical principles that have their origin in the Declaration of Helsinki, that are consistent with GCP according to International Conference on Harmonisation (ICH) guidelines, the applicable regulatory requirements(s) for the country in which the study was conducted, and applicable standard operating procedures (SOPs).

Background therapy:

NA

Evidence for comparator:

NA

Actual start date of recruitment	15 August 2011
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	Taiwan: 341
Worldwide total number of subjects	341
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)	202

Adolescents (12-17 years)	128
Adults (18-64 years)	11
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were enrolled at three study centers in Taiwan.

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	Not applicable
Blinding used	Not blinded

Blinding implementation details:

NA

Arms

Are arms mutually exclusive?	Yes
Arm title	ACWY 2-10 Yrs

Arm description:

Subjects 2-10 years of age received one MenACWY-CRM vaccination

Arm type	Experimental
Investigational medicinal product name	MenACWY-CRM
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Single 0.5 mL dose of MenACWY-CRM was administered by IM injection.

Arm title	ACWY 11-18 Yrs

Arm description:

Subjects 11-18 years of age received one MenACWY-CRM vaccination

Arm type	Experimental
Investigational medicinal product name	MenACWY-CRM
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Single 0.5 mL dose of MenACWY-CRM was administered by IM injection.

Number of subjects in period 1	ACWY 2-10 Yrs	ACWY 11-18 Yrs
Started	173	168
Completed	173	167
Not completed	0	1
Consent withdrawn by subject	-	1

Baseline characteristics

Reporting groups	
Reporting group title	ACWY 2-10 Yrs
Reporting group description:	
Subjects 2-10 years of age received one MenACWY-CRM vaccination	
Reporting group title	ACWY 11-18 Yrs
Reporting group description:	
Subjects 11-18 years of age received one MenACWY-CRM vaccination	

Reporting group values	ACWY 2-10 Yrs	ACWY 11-18 Yrs	Total
Number of subjects	173	168	341
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)	0	0	0
Children (2-11 years)	173	29	202
Adolescents (12-17 years)	0	128	128
Adults (18-64 years)	0	11	11
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	6.3	14	
standard deviation	± 2.6	± 2.2	-
Gender categorical Units: Subjects			
Female	92	88	180
Male	81	80	161

End points

End points reporting groups

Reporting group title	ACWY 2-10 Yrs
Reporting group description:	
Subjects 2-10 years of age received one MenACWY-CRM vaccination	
Reporting group title	ACWY 11-18 Yrs
Reporting group description:	
Subjects 11-18 years of age received one MenACWY-CRM vaccination	
Subject analysis set title	All Enrolled Population
Subject analysis set type	Full analysis
Subject analysis set description:	
All subjects who have signed an informed consent, undergone screening procedure(s), and have a subject number assigned.	
Subject analysis set title	Modified Intention-to-treat (MITT) population, Immunogenicity
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
This population is defined by visit (visit 1, visit 2, both visits) and by serogroup. All subjects in the exposed population who provided evaluable serum samples whose assay results are available for at least one serogroup on Day 1 and/or Day 29	
Subject analysis set title	ACWY 2-5 Yrs
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
Subjects 2 to 5 years of age received one MenACWY-CRM vaccination	
Subject analysis set title	Overall (2 - 18 Yrs)
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
Subjects 2 to 8 years of age received one MenACWY-CRM vaccination	
Subject analysis set title	ACWY 6-10 Yrs
Subject analysis set type	Safety analysis
Subject analysis set description:	
Subjects 6-10 years of age received one MenACWY-CRM vaccination	
Subject analysis set title	ACWY 11- 18 Yrs
Subject analysis set type	Safety analysis
Subject analysis set description:	
Subjects 11-18 years of age received one MenACWY-CRM vaccination	
Subject analysis set title	Overall (6-18 Yrs)
Subject analysis set type	Safety analysis
Subject analysis set description:	
Subjects 6-18 years of age received one MenACWY-CRM vaccination	

Primary: 1. Percentage of Overall Subjects With Seroresponse, Directed Against Neisseria meningitidis Serogroups A, C, W and Y After MenACWY-CRM Vaccination.

End point title	1. Percentage of Overall Subjects With Seroresponse, Directed Against Neisseria meningitidis Serogroups A, C, W and Y After MenACWY-CRM Vaccination.[1]

End point description:

Immunogenicity was measured as the percentage of subjects with human serum bactericidal assay (hSBA) seroresponse and associated 95% Clopper-Pearson confidence interval (CI), directed against N. meningitidis serogroups A, C, W and Y, evaluated by serum bactericidal assay using human complement (hSBA), at 28 days after one vaccination of MenACWY-CRM (day 29).
Seroresponse is defined as:
a. for subjects with a prevaccination hSBA titer <1:4, a postvaccination hSBA titer ≥1:8.
b. for subjects with a prevaccination hSBA titer ≥1:4, an increase in hSBA titer of at least four times the

prevaccination titer.
Analysis was done on modified intention-to-treat (MITT) population.

End point type	Primary

End point timeframe:

Day 29

Notes:

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

End point values	Overall (2 - 18 Yrs)			
Subject group type	Subject analysis set			
Number of subjects analysed	335			
Units: Percentage of subjects				
number (confidence interval 95%)				
MenA	83 (79 to 87)			
MenC (N= 333)	93 (90 to 96)			
MenW (N=334)	50 (45 to 55)			
MenY (N= 333)	65 (60 to 70)			

Statistical analyses

No statistical analyses for this end point

Secondary: 2. Percentage of Subjects With Seroresponse, Directed Against N. Meningitidis Serogroups A, C, W and Y After MenACWY-CRM Vaccination, by Age Group

End point title	2. Percentage of Subjects With Seroresponse, Directed Against N. Meningitidis Serogroups A, C, W and Y After MenACWY-CRM Vaccination, by Age Group

End point description:

Immunogenicity was measured as the percentage of subjects with hSBA response and associated 95% CI, directed against N. meningitidis serogroups A, C, W and Y, at Day 29, by age groups.
Analysis was done on modified intention-to-treat (MITT) population.

End point type	Secondary

End point timeframe:

Day 29

End point values	ACWY 2-10 Yrs	ACWY 11-18 Yrs		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	170	166		
Units: Percentage of Subjects				
number (confidence interval 95%)				
Men A (N=170,165)	77 (70 to 83)	89 (83 to 93)		
MenC (N=167,166)	92 (86 to 95)	95 (90 to 97)		
MenW (N=168,166)	54 (46 to 62)	46 (38 to 54)		
MenY (N=167,166)	61 (53 to 69)	69 (62 to 76)		

Statistical analyses

No statistical analyses for this end point

Secondary: 3. Geometric Mean Titers (GMTs) of Subjects, Directed Against N. meningitidis Serogroups A, C, W and Y After MenACWY-CRM Vaccination.

End point title	3. Geometric Mean Titers (GMTs) of Subjects, Directed Against N. meningitidis Serogroups A, C, W and Y After MenACWY-CRM Vaccination.

End point description:

Immunogenicity was measured as hSBA GMTs and associated 95% CI, against N. meningitidis serogroups A, C, W and Y, before the vaccination (Day 1) and 28 days after MenACWY-CRM vaccination (Day 29), by age group and overall.
Analysis was done on MITT population.

End point type	Secondary

End point timeframe:

Day 1 and Day 29

End point values	ACWY 2-10 Yrs	ACWY 11-18 Yrs	Overall (2 - 18 Yrs)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	170	165	335	
Units: Titers				
geometric mean (confidence interval 95%)				
MenA (Day 1)	2.05 (1.92 to 2.2)	2.2 (2.05 to 2.36)	2.12 (2.02 to 2.24)	
MenC (Day 1) (N=167,166,333)	2.66 (2.35 to 3.02)	3.64 (3.21 to 4.12)	3.11 (2.83 to 3.42)	
MenW (Day 1) (N=168,166,334)	7.32 (5.65 to 9.49)	15 (12 to 19)	10 (8.62 to 13)	
MenY (Day 1) (N=167,166,333)	3.21 (2.69 to 3.83)	3.95 (3.31 to 4.71)	3.56 (3.12 to 4.06)	
MenA (Day 29)	32 (24 to 43)	88 (66 to 117)	53 (42 to 65)	
MenC (Day 29) (N=167,166,333)	117 (93 to 147)	273 (218 to 342)	179 (151 to 211)	
MenW (Day 29) (N=168,166,334)	49 (40 to 60)	104 (85 to 127)	71 (61 to 82)	
MenY (Day 29) (N=167,166,333)	26 (20 to 33)	56 (43 to 72)	38 (31 to 46)	

Statistical analyses

No statistical analyses for this end point

Secondary: 4. Geometric Mean Ratios (GMRs) of Subjects, Directed Against N. meningitidis Serogroups A, C, W and Y After MenACWY-CRM Vaccination.

End point title	4. Geometric Mean Ratios (GMRs) of Subjects, Directed Against N. meningitidis Serogroups A, C, W and Y After MenACWY-CRM Vaccination.

End point description:

Immunogenicity was measured as ratio of postvaccination GMTs to prevaccination GMTs and associated 95% CI, against N. meningitidis serogroups A, C, W and Y, at 28 days after MenACWY-CRM vaccination (Day 29), by age group and overall.
Analysis was done on MITT population.

End point type	Secondary

End point timeframe:

Day 29 post-vaccination / Day 1 pre-vaccination

End point values	ACWY 2-10 Yrs	ACWY 11-18 Yrs	Overall (2 - 18 Yrs)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	170	165	335	
Units: Ratio				
geometric mean (confidence interval 95%)				
MenA	16 (12 to 21)	40 (30 to 53)	25 (20 to 31)	
MenC (N=167,166,333)	44 (35 to 56)	75 (59 to 95)	57 (48 to 69)	
MenW (N=168,166,334)	6.66 (5.19 to 8.5)	6.91 (5.39 to 8.85)	6.78 (5.63 to 8.16)	
MenY (N=167,166,333)	8.02 (6.09 to 11)	14 (11 to 19)	11 (8.67 to 13)	

Statistical analyses

No statistical analyses for this end point

Secondary: 5. Percentage of Subjects With hSBA Titer ≥1:8, Directed Against N. meningitidis Serogroups A, C, W and Y After MenACWY-CRM Vaccination.

End point title	5. Percentage of Subjects With hSBA Titer ≥1:8, Directed Against N. meningitidis Serogroups A, C, W and Y After MenACWY-CRM Vaccination.

End point description:

Immunogenicity was measured as the percentage of subjects with hSBA titer ≥1:8 and associated 95% CI, before vaccination (Day 1) and 28 days after MenACWYCRM vaccination (Day 29), bye age group and overall.
Analysis was done on MITT population.

End point type	Secondary

End point timeframe:

Day 1 and Day 29

End point values	ACWY 2-10 Yrs	ACWY 11-18 Yrs	Overall (2 - 18 Yrs)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	170	165	335	
Units: Percentage of Subjects				
number (confidence interval 95%)				
MenA (Day 1)	1 (0 to 4)	4 (2 to 9)	3 (1 to 5)	
MenC (Day 1) (N=167,166,333)	11 (7 to 17)	23 (17 to 31)	17 (13 to 22)	
MenW (Day 1) (N=168,166,334)	47 (39 to 55)	70 (62 to 77)	58 (53 to 64)	
MenY (Day 1) (N=167,166,333)	22 (16 to 29)	26 (19 to 33)	24 (19 to 29)	
MenA (Day 29)	77 (70 to 83)	90 (84 to 94)	83 (79 to 87)	
MenC (Day 29) (N=167,166,333)	95 (90 to 98)	98 (95 to 100)	96 (94 to 98)	
MenW (Day 29) (N=168,166,334)	93 (88 to 96)	99 (96 to 100)	96 (93 to 98)	
MenY (Day 290) (N=167,166,333)	78 (71 to 84)	86 (79 to 91)	82 (77 to 86)	

Statistical analyses

No statistical analyses for this end point

Secondary: 6. Number of Subjects Who Reported Solicited Local and Systemic Adverse Events After MenACWY-CRM Vaccination, Age 2 to 5 Years.

End point title	6. Number of Subjects Who Reported Solicited Local and Systemic Adverse Events After MenACWY-CRM Vaccination, Age 2 to 5 Years.

End point description:

Safety was assessed as the number of subjects aged 2 to 5 years who reported solicited local and systemic adverse events (AEs) within days 1 through 7 after MenACWY-CRM vaccination.
Analysis was done on safety population.

End point type	Secondary

End point timeframe:

From Day 1 through Day 7 postvaccination

End point values	ACWY 2-5 Yrs			
Subject group type	Subject analysis set			
Number of subjects analysed	72			
Units: Number of Subjects				
Injection site tenderness	27			
Injection site erythema	7			
Injection site induration	6			
Change in eating habits	2			
Sleepiness	3			
Irritability	5			
Vomiting	7			
Diarrhea	2			
Rash - Any	4			
Rash - Urticarial	1			
Fever (≥38°C)	4			
Temperature >= 40 C	0			

Analges. Antipyr. Meds	4			

Statistical analyses

No statistical analyses for this end point

Secondary: 7. Number of Subjects Who Reported Solicited Local and Systemic Adverse Events After MenACWY-CRM Vaccination, Age 6 to 18 Years.

End point title	7. Number of Subjects Who Reported Solicited Local and Systemic Adverse Events After MenACWY-CRM Vaccination, Age 6 to 18 Years.

End point description:

Safety was assessed as the number of subjects aged 6 to 18 years who reported solicited local and systemic AEs within days 1 through 7 after MenACWY-CRM vaccination.
Analysis was done on safety population.

End point type	Secondary

End point timeframe:

From Day 1 through Day 7 postvaccination

End point values	ACWY 6-10 Yrs	ACWY 11- 18 Yrs	Overall (6-18 Yrs)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	101	167	268	
Units: Number of Subjects				
Injection site pain	37	62	99	
Injection site erythema	17	17	34	
Injection site induration	14	12	26	
Chills	2	6	8	
Nausea	10	10	20	
Malaise	13	35	48	
Myalgia	20	49	69	
Arthralgia	3	13	16	
Headache	11	29	40	
Rash - Any	7	4	11	
Rash - Urticarial	3	3	6	
Fever (≥38°C)	3	2	5	

Statistical analyses

No statistical analyses for this end point

Secondary: 8. Number of Subjects Reporting Unsolicited AEs, After Men ACWY-CRM Vaccination, Age 2 to 18 Years.

End point title	8. Number of Subjects Reporting Unsolicited AEs, After Men

	ACWY-CRM Vaccination, Age 2 to 18 Years.

End point description:

Safety was assessed as the number of subjects aged 2 to 18 years who reported unsolicited AEs within days 1 through 7 after MenACWY-CRM vaccination.
Analysis was done on safety population.

End point type	Secondary

End point timeframe:

From Day 1 through Day 7 postvaccination

End point values	ACWY 2-10 Yrs	ACWY 11-18 Yrs	Overall (2 - 18 Yrs)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	170	165	335	
Units: Number of Subjects				
Any adverse event (AE)	27	20	47	
At least possibly related AEs	11	10	21	
Any SAE	1	0	1	
Possibly/Probably related SAE	0	0	0	
AE leading to withdrawal	0	0	0	
Medically attended AEs	49	20	69	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Throughout the study period (from Day 1 through Day 29).	
Adverse event reporting additional description:	
A systematic adverse event is equivalent to an event that was solicited by the diary card, whereas a non-systematic event is equivalent to an event that was not solicited by the diary card.	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups	
Reporting group title	ACWY 2-10 Yrs
Reporting group description:	
Subjects 2-10 years of age received one MenACWY-CRM vaccination.	
Reporting group title	ACWY 11-18 Yrs
Reporting group description:	
Subjects 11-18 years of age received one MenACWY-CRM vaccination.	
Reporting group title	Overall (2 - 18 Years)
Reporting group description:	
Subjects 2 to 18 years of age received one MenACWY-CRM vaccination.	

Serious adverse events	ACWY 2-10 Yrs	ACWY 11-18 Yrs	Overall (2 - 18 Years)
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 173 (0.58%)	0 / 167 (0.00%)	1 / 340 (0.29%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 173 (0.58%)	0 / 167 (0.00%)	1 / 340 (0.29%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	ACWY 2-10 Yrs	ACWY 11-18 Yrs	Overall (2 - 18 Years)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	110 / 173 (63.58%)	98 / 167 (58.68%)	208 / 340 (61.18%)
Nervous system disorders			

Headache			
subjects affected / exposed	13 / 173 (7.51%)	29 / 167 (17.37%)	42 / 340 (12.35%)
occurrences (all)	15	36	51
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	58 / 173 (33.53%)	43 / 167 (25.75%)	101 / 340 (29.71%)
occurrences (all)	61	45	106
Injection site induration			
subjects affected / exposed	49 / 173 (28.32%)	36 / 167 (21.56%)	85 / 340 (25.00%)
occurrences (all)	53	40	93
Injection site pain			
subjects affected / exposed	64 / 173 (36.99%)	62 / 167 (37.13%)	126 / 340 (37.06%)
occurrences (all)	65	62	127
Malaise			
subjects affected / exposed	13 / 173 (7.51%)	35 / 167 (20.96%)	48 / 340 (14.12%)
occurrences (all)	15	38	53
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	10 / 173 (5.78%)	10 / 167 (5.99%)	20 / 340 (5.88%)
occurrences (all)	11	11	22
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	11 / 173 (6.36%)	4 / 167 (2.40%)	15 / 340 (4.41%)
occurrences (all)	12	4	16
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 173 (1.73%)	13 / 167 (7.78%)	16 / 340 (4.71%)
occurrences (all)	3	15	18
Myalgia			
subjects affected / exposed	20 / 173 (11.56%)	49 / 167 (29.34%)	69 / 340 (20.29%)
occurrences (all)	21	51	72
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	10 / 173 (5.78%)	2 / 167 (1.20%)	12 / 340 (3.53%)
occurrences (all)	10	2	12
Upper respiratory tract infection			

subjects affected / exposed occurrences (all)	16 / 173 (9.25%) 17	6 / 167 (3.59%) 6	22 / 340 (6.47%) 23

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 May 2011	The protocol amendment was implemented before first subject has entered the study and consisted of the change of the MenACWY-CRM presentation, instead of prefilled syringe; vial-vial presentation was introduced and used.

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.

Not specified

Notes: