



Clinical trial results:

A Phase IV, Open-label, Controlled, Multi-center Study to Evaluate the 5-year Antibody Persistence Among Children Who Previously Received Novartis MenACWY Conjugate Vaccine at 2 to 10 Years of Age and to Assess the Immune Response to a Single Dose of Novartis MenACWY Conjugate Vaccine.

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

Summary

EudraCT number	2014-004446-95
Trial protocol	Outside EU/EEA
Global end of trial date	15 June 2014

Results information

Result version number	v2 (current)
This version publication date	04 June 2016
First version publication date	01 February 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	V59P20E1
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01823536
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Vaccines & Diagnostics, Srl
Sponsor organisation address	350 Massachusetts Avenue, Massachusetts, United States, 02139
Public contact	Posting Director, Novartis Vaccines & Diagnostics, Srl, RegistryContactVaccinesUS@novartis.com
Scientific contact	Posting Director, Novartis Vaccines & Diagnostics, Srl, 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
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Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	16 June 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	15 June 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the persistence of the antibody response at 5 years postvaccination in children who previously received one or two doses of MenACWY in study V59P20, as measured by percentage of subjects with human Serum Bactericidal Assay (hSBA) $\geq 1:8$ directed against N. meningitidis serogroups A, C, W-135, and Y.

Protection of trial subjects:

Study vaccines were not administered to individuals with known hypersensitivity to any component of the vaccines.

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 was not injected into a blood vessel.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 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	United States: 465
Worldwide total number of subjects	465
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)	368
Adolescents (12-17 years)	97
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 22 study sites in United States.

Pre-assignment

Screening details:

All 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	7-10_ACWY_2

Arm description:

Subjects who had previously received 2 injections of MenACWY-CRM vaccine at 2-5 years of age, were administered 1 injection of MenACWY-CRM vaccine at 7-10 years of age.

Arm type	Experimental
Investigational medicinal product name	Meningococcal (groups A, C, W, and Y) oligosaccharide diphtheria CRM-197
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Each dose 0.5 mL of injectable solution was administered intramuscularly.

Arm title	7-10_ACWY_1
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Arm description:

Subjects who had previously received 1 injection of MenACWY-CRM vaccine at 2-5 years of age, were administered 1 injection of MenACWY-CRM vaccine at 7-10 years of age.

Arm type	Experimental
Investigational medicinal product name	Meningococcal (groups A, C, W, and Y) oligosaccharide diphtheria CRM-197
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Each dose 0.5 mL of injectable solution was administered intramuscularly.

Arm title	7-10_Vaccine naive
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Arm description:

Vaccine naive subjects, age-matched to the 7-10 years of age groups, received 1 injection of MenACWY-CRM vaccine.

Arm type	Experimental
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Investigational medicinal product name	Meningococcal (groups A, C, W, and Y) oligosaccharide diphtheria CRM-197
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
Each dose 0.5 mL of injectable solution was administered intramuscularly.	
Arm title	11-15_ACWY_1
Arm description:	
Subjects who had previously received 1 injection of MenACWY-CRM vaccine at 6-10 years of age, were administered 1 injection of MenACWY-CRM vaccine at 11-15 years of age.	
Arm type	Experimental
Investigational medicinal product name	Meningococcal (groups A, C, W, and Y) oligosaccharide diphtheria CRM-197
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
Each dose 0.5 mL of injectable solution was administered intramuscularly.	
Arm title	11-15_Vaccine naive
Arm description:	
Vaccine naive subjects, age-matched to the ≥ 11 - ≤ 15 years of age group, received 1 injection of MenACWY-CRM vaccine	
Arm type	Experimental
Investigational medicinal product name	Meningococcal (groups A, C, W, and Y) oligosaccharide diphtheria CRM-197
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
Each dose 0.5 mL of injectable solution was administered intramuscularly.	
Arm title	Not Assigned
Arm description:	
Randomized to receive another meningococcal ACWY vaccine in the parent study and hence not eligible for enrolment	
Arm type	Experimental
Investigational medicinal product name	Meningococcal (groups A, C, W, and Y) oligosaccharide diphtheria CRM-197
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
Each dose 0.5 mL of injectable solution was administered intramuscularly.	

Number of subjects in period 1	7-10_ACWY_2	7-10_ACWY_1	7-10_Vaccine naive
Started	73	103	120
Completed	71	101	119
Not completed	2	2	1
Consent withdrawn by subject	1	1	-
Lost to follow-up	1	-	-
Premature withdrawal	-	-	1
Protocol deviation	-	1	-

Number of subjects in period 1	11-15_ACWY_1	11-15_Vaccine naive	Not Assigned
Started	66	101	2
Completed	64	99	2
Not completed	2	2	0
Consent withdrawn by subject	-	-	-
Lost to follow-up	1	1	-
Premature withdrawal	1	1	-
Protocol deviation	-	-	-

Baseline characteristics

Reporting groups

Reporting group title	7-10_ACWY_2
Reporting group description: Subjects who had previously received 2 injections of MenACWY-CRM vaccine at 2-5 years of age, were administered 1 injection of MenACWY-CRM vaccine at 7-10 years of age.	
Reporting group title	7-10_ACWY_1
Reporting group description: Subjects who had previously received 1 injection of MenACWY-CRM vaccine at 2-5 years of age, were administered 1 injection of MenACWY-CRM vaccine at 7-10 years of age.	
Reporting group title	7-10_Vaccine naive
Reporting group description: Vaccine naive subjects, age-matched to the 7-10 years of age groups, received 1 injection of MenACWY-CRM vaccine.	
Reporting group title	11-15_ACWY_1
Reporting group description: Subjects who had previously received 1 injection of MenACWY-CRM vaccine at 6-10 years of age, were administered 1 injection of MenACWY-CRM vaccine at 11-15 years of age.	
Reporting group title	11-15_Vaccine naive
Reporting group description: Vaccine naive subjects, age-matched to the ≥ 11 - ≤ 15 years of age group, received 1 injection of MenACWY-CRM vaccine	
Reporting group title	Not Assigned
Reporting group description: Randomized to receive another meningococcal ACWY vaccine in the parent study and hence not eligible for enrolment	

Reporting group values	7-10_ACWY_2	7-10_ACWY_1	7-10_Vaccine naive
Number of subjects	73	103	120
Age categorical Units: Subjects			

Age continuous Units: months arithmetic mean standard deviation	8.3 ± 1.1	8.1 ± 1.2	8.5 ± 1.1
Gender categorical Units: Subjects			
Female	35	49	63
Male	38	54	57

Reporting group values	11-15_ACWY_1	11-15_Vaccine naive	Not Assigned
Number of subjects	66	101	2
Age categorical Units: Subjects			

Age continuous Units: months arithmetic mean	13	11.8	8
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standard deviation	± 1.6	± 1	± 1.4
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Gender categorical Units: Subjects			
Female	28	46	1
Male	38	55	1

Reporting group values	Total		
Number of subjects	465		
Age categorical Units: Subjects			

Age continuous Units: months arithmetic mean standard deviation	-		
Gender categorical Units: Subjects			
Female	222		
Male	243		

End points

End points reporting groups

Reporting group title	7-10_ACWY_2
Reporting group description: Subjects who had previously received 2 injections of MenACWY-CRM vaccine at 2-5 years of age, were administered 1 injection of MenACWY-CRM vaccine at 7-10 years of age.	
Reporting group title	7-10_ACWY_1
Reporting group description: Subjects who had previously received 1 injection of MenACWY-CRM vaccine at 2-5 years of age, were administered 1 injection of MenACWY-CRM vaccine at 7-10 years of age.	
Reporting group title	7-10_Vaccine naive
Reporting group description: Vaccine naive subjects, age-matched to the 7-10 years of age groups, received 1 injection of MenACWY-CRM vaccine.	
Reporting group title	11-15_ACWY_1
Reporting group description: Subjects who had previously received 1 injection of MenACWY-CRM vaccine at 6-10 years of age, were administered 1 injection of MenACWY-CRM vaccine at 11-15 years of age.	
Reporting group title	11-15_Vaccine naive
Reporting group description: Vaccine naive subjects, age-matched to the ≥ 11 - ≤ 15 years of age group, received 1 injection of MenACWY-CRM vaccine	
Reporting group title	Not Assigned
Reporting group description: Randomized to receive another meningococcal ACWY vaccine in the parent study and hence not eligible for enrolment	
Subject analysis set title	All Enrolled Set
Subject analysis set type	Full analysis
Subject analysis set description: All screened subjects who provided informed consent and provided demographic and/or baseline screening assessments, regardless of the treatment status in the trial and received a subject ID.	
Subject analysis set title	Day 1 FAS
Subject analysis set type	Full analysis
Subject analysis set description: All subjects in the enrolled population who provided immunogenicity data on day 1.	
Subject analysis set title	Day 28 FAS
Subject analysis set type	Full analysis
Subject analysis set description: All subjects in the enrolled population who received a study vaccination and provided immunogenicity data on day 28.	
Subject analysis set title	Day 1 Per protocol set (PPS)
Subject analysis set type	Per protocol
Subject analysis set description: All subjects in the day 1 FAS immunogenicity population who had no major protocol deviations as defined prior to analysis and were not excluded due to other reasons defined prior to analysis.	
Subject analysis set title	Day 28 PPS
Subject analysis set type	Per protocol
Subject analysis set description: All subjects in the day 28 FAS immunogenicity population who had no major protocol deviations as defined prior to analysis and were not excluded due to other reasons defined prior to analysis.	

Primary: 1. Percentages of Subjects With Persisting hSBA Titers $\geq 1:8$ Against *Neisseria Meningitidis* (N.Meningitidis) Serogroups A, C, W and Y, Five Years After Having Received One or Two Doses of MenACWY-CRM Vaccine

End point title	1. Percentages of Subjects With Persisting hSBA Titers $\geq 1:8$ Against <i>Neisseria Meningitidis</i> (N.Meningitidis) Serogroups A, C, W and Y, Five Years After Having Received One or Two Doses of MenACWY-CRM Vaccine ^{[1][2]}
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End point description:

The percentages of subjects with persisting serum bactericidal antibody $\geq 1:8$, against N.meningitidis serogroups A, C, W and Y, after having received one or two doses of MenACWY-CRM vaccine, five years earlier in the parent study, are reported.

The serum bactericidal antibodies directed against N.meningitidis serogroups, are measured by human complement Serum Bactericidal Assay (hSBA).

The analysis was done on per-protocol population

End point type	Primary
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End point timeframe:

5 years post 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 analysis is associated to this endpoint.

[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 analysis is associated to this endpoint.

End point values	7-10_ACWY_2	7-10_ACWY_1	11-15_ACWY_1	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	70	96	64	
Units: Percentage of subjects				
number (confidence interval 95%)				
Men A (N=68, 96, 64)	7 (2 to 16)	14 (7 to 22)	22 (13 to 34)	
Men C (N=69, 96, 64)	48 (36 to 60)	32 (23 to 43)	56 (43 to 69)	
Men W-135 (N=69, 96, 64)	83 (72 to 91)	74 (64 to 82)	80 (68 to 89)	
Men Y (N=70, 96, 64)	50 (38 to 62)	48 (38 to 58)	53 (40 to 66)	

Statistical analyses

No statistical analyses for this end point

Secondary: 2. Persisting Geometric Mean Titers Against N. meningitidis Serogroups A, C, W and Y in Subjects, Five Years After Having Received One or Two Doses of MenACWY-CRM Vaccine.

End point title	2. Persisting Geometric Mean Titers Against N. meningitidis Serogroups A, C, W and Y in Subjects, Five Years After Having Received One or Two Doses of MenACWY-CRM Vaccine. ^[3]
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End point description:

The persistence of geometric mean titers (GMTs) against N.meningitidis serogroups A, C, W and Y in subjects who had received one or two doses of MenACWY-CRM vaccine, five years earlier in the parent study, are reported.

The analysis was done on per-protocol population.

End point type	Secondary
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End point timeframe:

5 years post-vaccination

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 is associated to this endpoint.

End point values	7-10_ACWY_2	7-10_ACWY_1	11-15_ACWY_1	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	70	96	64	
Units: Titers				
geometric mean (confidence interval 95%)				
Men A (N= 68, 96, 64)	2.41 (2.09 to 2.78)	2.95 (2.42 to 3.61)	3.73 (2.74 to 5.06)	
Men C (N= 69, 96, 64)	7.55 (5.44 to 10)	6.5 (4.75 to 8.9)	12 (7.72 to 19)	
Men W (N= 69, 96, 64)	23 (17 to 31)	19 (14 to 25)	26 (18 to 38)	
Men Y	8.57 (6.08 to 12)	8.13 (6.11 to 11)	10 (6.51 to 16)	

Statistical analyses

No statistical analyses for this end point

Secondary: 3. Percentages of Subjects With Persisting hSBA Titers $\geq 1:8$ Against N.Meningitidis Serogroups A, C, W and Y as Compared to Age Matched Vaccine-naïve Subjects

End point title	3. Percentages of Subjects With Persisting hSBA Titers $\geq 1:8$ Against N.Meningitidis Serogroups A, C, W and Y as Compared to Age Matched Vaccine-naïve Subjects ^[4]
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End point description:

The percentages of subjects with persisting serum bactericidal antibody $\geq 1:8$, against N.meningitidis serogroups A, C, W and Y, after having received one or two doses of MenACWY-CRM vaccine five years earlier in the parent study, are compared with the hSBA response in age matched vaccine-naïve subjects.

The analysis was done on per protocol population.

End point type	Secondary
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End point timeframe:

5 years post-vaccination; baseline for naïve

Notes:

[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 analysis is associated to this endpoint.

End point values	7-10_ACWY_2	7-10_ACWY_1	7-10_Vaccine naïve	11-15_ACWY_1
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	70	96	118	64
Units: Percentage of subjects				
number (confidence interval 95%)				
Men A (N= 68, 96, 118, 64, 100)	7 (2 to 16)	14 (7 to 22)	0 (0 to 3)	22 (13 to 34)
Men C (N= 69, 96, 118, 64, 99)	48 (36 to 60)	32 (23 to 43)	21 (14 to 30)	56 (43 to 69)
Men W (N= 69, 96, 118, 64, 100)	83 (72 to 91)	75 (64 to 82)	52 (42 to 61)	80 (68 to 89)
Men Y	50 (38 to 62)	48 (38 to 58)	23 (16 to 32)	53 (40 to 66)

End point values	11-15_Vaccine naive			
Subject group type	Reporting group			
Number of subjects analysed	100			
Units: Percentage of subjects				
number (confidence interval 95%)				
Men A (N= 68, 96, 118, 64, 100)	5 (2 to 11)			
Men C (N= 69, 96, 118, 64, 99)	21 (14 to 31)			
Men W (N= 69, 96, 118, 64, 100)	54 (44 to 64)			
Men Y	37 (28 to 47)			

Statistical analyses

No statistical analyses for this end point

Secondary: 4. Percentages of Subjects With hSBA Titers $\geq 1:8$ Against N.Meningitidis Serogroups A, C, W and Y, After Receiving One Injection of MenACWY-CRM Vaccine in the Present Study.

End point title	4. Percentages of Subjects With hSBA Titers $\geq 1:8$ Against N.Meningitidis Serogroups A, C, W and Y, After Receiving One Injection of MenACWY-CRM Vaccine in the Present Study. ^[5]
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End point description:

The antibody response against N.meningitidis serogroups A, C, W and Y, at one month after one injection of Men ACWY-CRM vaccine was administered in the present study to subjects who had received either one or two doses of MenACWY-CRM vaccine 5 years earlier and to age matched naive subjects, is evaluated in terms of the percentages of subjects with hSBA titers $\geq 1:8$.
The analysis was done on per protocol population.

End point type	Secondary
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End point timeframe:

Day 28 post-vaccination

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 is associated to this endpoint.

End point values	7-10_ACWY_2	7-10_ACWY_1	7-10_Vaccine naive	11-15_ACWY_1
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	65	95	110	60
Units: Percentage of subjects				
number (confidence interval 95%)				
Men A (N= 63, 95, 109, 60, 85)	98 (91 to 100)	100 (96 to 100)	75 (66 to 83)	100 (94 to 100)
Men C (N= 65, 94, 109, 60, 85)	100 (94 to 100)	100 (96 to 100)	82 (73 to 88)	100 (94 to 100)
Men W (N= 63, 95, 110, 60, 85)	100 (94 to 100)	100 (96 to 100)	94 (87 to 97)	100 (94 to 100)
men Y (N= 65, 94, 110, 59, 85)	100 (94 to 100)	100 (96 to 100)	85 (77 to 91)	100 (94 to 100)

End point values	11-15_Vaccine naive			
Subject group type	Reporting group			
Number of subjects analysed	85			
Units: Percentage of subjects				
number (confidence interval 95%)				
Men A (N= 63, 95, 109, 60, 85)	80 (70 to 88)			
Men C (N= 65, 94, 109, 60, 85)	86 (77 to 92)			
Men W (N= 63, 95, 110, 60, 85)	92 (84 to 97)			
men Y (N= 65, 94, 110, 59, 85)	82 (73 to 90)			

Statistical analyses

No statistical analyses for this end point

Secondary: 5. Geometric Mean Titers Against N.Meningitidis Serogroups A, C, W and Y, After Receiving One Injection of MenACWY-CRM Vaccine in the Present Study.

End point title	5. Geometric Mean Titers Against N.Meningitidis Serogroups A, C, W and Y, After Receiving One Injection of MenACWY-CRM Vaccine in the Present Study. ^[6]
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End point description:

The antibody response against N.meningitidis serogroups A, C, W and Y, at one month after one injection of Men ACWY-CRM vaccine was administered in the present study to subjects who had received either one or two doses of MenACWY-CRM vaccine 5 years earlier and to age matched naive subjects, is evaluated in terms of GMTs.

The analysis was done on per-protocol population.

End point type	Secondary
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End point timeframe:

Day 28 post vaccination

Notes:

[6] - 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 is associated to this endpoint.

End point values	7-10_ACWY_2	7-10_ACWY_1	7-10_Vaccine naive	11-15_ACWY_1
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	65	95	110	60
Units: Titers				
geometric mean (confidence interval 95%)				
Men A (N= 63, 95, 109, 60, 85)	321 (241 to 428)	361 (299 to 436)	28 (20 to 39)	350 (265 to 463)
Men C (N= 65, 94, 109, 60, 85)	760 (545 to 1059)	498 (406 to 610)	48 (33 to 70)	712 (490 to 1036)
Men W (N= 63, 95, 110, 60, 85)	1571 (1247 to 1980)	1534 (1255 to 1873)	55 (42 to 72)	1556 (1083 to 2237)
Men Y (N= 65, 94, 110, 59, 85)	1286 (992 to 1668)	1693 (1360 to 2107)	48 (34 to 66)	1442 (1050 to 1979)

End point values	11-15_Vaccine naive			
Subject group type	Reporting group			
Number of subjects analysed	85			
Units: Titers				
geometric mean (confidence interval 95%)				
Men A (N= 63, 95, 109, 60, 85)	31 (22 to 45)			
Men C (N= 65, 94, 109, 60, 85)	102 (63 to 166)			
Men W (N= 63, 95, 110, 60, 85)	69 (48 to 99)			
Men Y (N= 65, 94, 110, 59, 85)	45 (30 to 69)			

Statistical analyses

No statistical analyses for this end point

Secondary: 6. Number of Subjects Reporting Solicited Adverse Events, After Receiving One Injection of MenACWY-CRM Vaccine in the Present Study.

End point title	6. Number of Subjects Reporting Solicited Adverse Events, After Receiving One Injection of MenACWY-CRM Vaccine in the Present Study. ^[7]
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End point description:

The number of subjects reporting solicited local and systemic adverse events after one injection of MenACWY-CRM vaccine was administered in the present study to Subjects, who had 5 years earlier received either one or two doses of MenACWY-CRM vaccine and Vaccine-naïve subjects.

The analysis was done on solicited safety set, ie, all subjects in the exposed set who provided post vaccination solicited reactogenicity data.

End point type	Secondary
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End point timeframe:

Day 1 to Day 7 post-vaccination

Notes:

[7] - 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 is associated to this endpoint.

End point values	7-10_ACWY_2	7-10_ACWY_1	7-10_Vaccine naive	11-15_ACWY_1
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	69	99	119	64
Units: Number of subjects				
Any local	46	61	59	38
Injection site pain (N= 68, 99, 117, 64, 98)	39	52	42	31
Injection site erythema (N= 68, 99, 117, 64, 98)	10	13	10	10
Injection site induration (N= 68, 99, 119, 64, 98)	12	12	7	7
Any Systemic	23	27	34	19
Chills (N= 68, 99, 117, 64, 98)	5	3	6	1

Malaise (N= 69, 99, 117, 64, 98)	15	14	13	11
Myalgia (N= 69, 99, 117, 64, 98)	9	8	8	4
Arthralgia (N= 69, 99, 117, 64, 98)	8	4	5	4
Headache (N= 69, 99, 117, 64, 97)	13	9	22	12
Nausea (N= 68, 99, 117, 64, 97)	10	11	12	7
Fever ($\geq 38^{\circ}\text{C}$; N= 66, 99, 115, 64, 96)	1	0	3	1
Prophyl. use analg/antip (N= 68, 99, 118, 63, 97)	0	1	2	1
Therapeutic use anal/antipyr.(N= 69,99,118,64,97)	11	12	11	11

End point values	11-15_Vaccine naive			
Subject group type	Reporting group			
Number of subjects analysed	98			
Units: Number of subjects				
Any local	52			
Injection site pain (N= 68, 99, 117, 64, 98)	47			
Injection site erythema (N= 68, 99, 117, 64, 98)	6			
Injection site induration (N= 68, 99, 119, 64, 98)	8			
Any Systemic	35			
Chills (N= 68, 99, 117, 64, 98)	2			
Malaise (N= 69, 99, 117, 64, 98)	19			
Myalgia (N= 69, 99, 117, 64, 98)	8			
Arthralgia (N= 69, 99, 117, 64, 98)	8			
Headache (N= 69, 99, 117, 64, 97)	21			
Nausea (N= 68, 99, 117, 64, 97)	8			
Fever ($\geq 38^{\circ}\text{C}$; N= 66, 99, 115, 64, 96)	0			
Prophyl. use analg/antip (N= 68, 99, 118, 63, 97)	1			
Therapeutic use anal/antipyr.(N= 69,99,118,64,97)	6			

Statistical analyses

No statistical analyses for this end point

Secondary: 7. Number of Subjects Reporting Unsolicited Adverse Events, After Receiving One Injection of MenACWY-CRM Vaccine in the Present Study.

End point title	7. Number of Subjects Reporting Unsolicited Adverse Events, After Receiving One Injection of MenACWY-CRM Vaccine in the Present Study. ^[8]
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End point description:

The safety and tolerability of one injection of MenACWY-CRM vaccine, administered in the present study, was evaluated in terms of the number of subjects reporting unsolicited adverse events, serious adverse events and adverse events leading to premature withdrawal.

The analysis was done on unsolicited safety set, ie, all exposed subjects who provided unsolicited adverse events (AE) data.

End point type	Secondary
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End point timeframe:

Day1 to Day 28 Postvaccination.

Notes:

[8] - 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 is associated to this endpoint.

End point values	7-10_ACWY_2	7-10_ACWY_1	7-10_Vaccine naive	11-15_ACWY_1
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	73	102	120	65
Units: Number of subjects				
Any adverse event (AE)	18	23	19	18
Possibly/Probably related unsolicited AE	4	3	4	7
Any SAE	0	0	1	0
Possibly/Probably related SAE	0	0	0	0
AE leading to withdrawal	0	0	0	0
Death	0	0	0	0

End point values	11-15_Vaccine naive			
Subject group type	Reporting group			
Number of subjects analysed	100			
Units: Number of subjects				
Any adverse event (AE)	11			
Possibly/Probably related unsolicited AE	5			
Any SAE	1			
Possibly/Probably related SAE	0			
AE leading to withdrawal	0			
Death	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All solicited AE were collected from day 1 to day 7; unsolicited AEs, AE's leading to premature withdrawal and all Serious Adverse Events were collected throughout the study (day1 to day 28).

Adverse event reporting additional description:

All solicited AEs are reported as systematic assessment; all unsolicited AEs are reported as non-systematic assessment. Serious adverse events analysis was done on the unsolicited safety set, other adverse events analysis was done on the overall safety set.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	17.1
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Reporting groups

Reporting group title	7-10_ACWY_1
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Reporting group description:

Subjects who had previously received 1 injection of MenACWY-CRM vaccine at 2-5 years of age, were administered 1 injection of MenACWY-CRM vaccine at 7-10 years of age.

Reporting group title	7-10_Vaccine naive
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Reporting group description:

Vaccine naive subjects, age-matched to the ≥ 7 - ≤ 10 years of age groups, received 1 injection of MenACWY-CRM vaccine.

Reporting group title	11-15_Vaccine naive
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Reporting group description:

Vaccine naive subjects, age-matched to the ≥ 11 - ≤ 15 years of age group, received 1 injection of MenACWY-CRM vaccine.

Reporting group title	11-15_ACWY_1
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Reporting group description:

Subjects who had previously received 1 injection of MenACWY-CRM vaccine at 6-10 years of age, were administered 1 injection of MenACWY-CRM vaccine at 11-15 years of age.

Reporting group title	7-10_ACWY_2
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Reporting group description:

Subjects who had previously received 2 injections of MenACWY-CRM vaccine at 2-5 years of age, were administered 1 injection of MenACWY-CRM vaccine at 7-10 years of age.

Serious adverse events	7-10_ACWY_1	7-10_Vaccine naive	11-15_Vaccine naive
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 102 (0.00%)	1 / 120 (0.83%)	1 / 100 (1.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	0 / 102 (0.00%)	1 / 120 (0.83%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Viral infection			
subjects affected / exposed	0 / 102 (0.00%)	0 / 120 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	11-15_ACWY_1	7-10_ACWY_2	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 65 (0.00%)	0 / 73 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	0 / 65 (0.00%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			
subjects affected / exposed	0 / 65 (0.00%)	0 / 73 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	7-10_ACWY_1	7-10_Vaccine naive	11-15_Vaccine naive
Total subjects affected by non-serious adverse events			
subjects affected / exposed	70 / 102 (68.63%)	77 / 120 (64.17%)	66 / 100 (66.00%)
Nervous system disorders			
Headache			
subjects affected / exposed	11 / 102 (10.78%)	23 / 120 (19.17%)	23 / 100 (23.00%)
occurrences (all)	13	31	26
General disorders and administration site conditions			
Chills			
subjects affected / exposed	3 / 102 (2.94%)	6 / 120 (5.00%)	2 / 100 (2.00%)
occurrences (all)	3	9	2
Injection site erythema			
subjects affected / exposed	34 / 102 (33.33%)	28 / 120 (23.33%)	21 / 100 (21.00%)
occurrences (all)	36	31	22

Injection site induration subjects affected / exposed occurrences (all)	26 / 102 (25.49%) 26	26 / 120 (21.67%) 27	17 / 100 (17.00%) 18
Injection site pain subjects affected / exposed occurrences (all)	57 / 102 (55.88%) 59	51 / 120 (42.50%) 56	52 / 100 (52.00%) 54
Malaise subjects affected / exposed occurrences (all)	14 / 102 (13.73%) 15	13 / 120 (10.83%) 14	19 / 100 (19.00%) 21
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all)	12 / 102 (11.76%) 14	14 / 120 (11.67%) 15	9 / 100 (9.00%) 13
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	5 / 102 (4.90%) 5	5 / 120 (4.17%) 6	9 / 100 (9.00%) 12
Myalgia subjects affected / exposed occurrences (all)	13 / 102 (12.75%) 13	10 / 120 (8.33%) 13	9 / 100 (9.00%) 9

Non-serious adverse events	11-15_ACWY_1	7-10_ACWY_2	
Total subjects affected by non-serious adverse events subjects affected / exposed	46 / 65 (70.77%)	48 / 73 (65.75%)	
Nervous system disorders Headache subjects affected / exposed occurrences (all)	15 / 65 (23.08%) 18	14 / 73 (19.18%) 17	
General disorders and administration site conditions Chills subjects affected / exposed occurrences (all)	2 / 65 (3.08%) 2	5 / 73 (6.85%) 6	
Injection site erythema subjects affected / exposed occurrences (all)	17 / 65 (26.15%) 17	25 / 73 (34.25%) 28	
Injection site induration			

subjects affected / exposed occurrences (all)	17 / 65 (26.15%) 18	21 / 73 (28.77%) 24	
Injection site pain subjects affected / exposed occurrences (all)	34 / 65 (52.31%) 35	42 / 73 (57.53%) 44	
Malaise subjects affected / exposed occurrences (all)	12 / 65 (18.46%) 13	15 / 73 (20.55%) 16	
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all)	8 / 65 (12.31%) 9	12 / 73 (16.44%) 14	
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	4 / 65 (6.15%) 6	8 / 73 (10.96%) 9	
Myalgia subjects affected / exposed occurrences (all)	4 / 65 (6.15%) 5	10 / 73 (13.70%) 12	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 January 2014	This amendment was done to change end of study definition and is defined as the completion of the testing of biological samples, to be achieved no later than 8 months after collection of the last biological sample visit at visit 2, day 28.

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:

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/20943209>