Clinical trial results:
A Phase 3b, Open-Label, Controlled, Multi-Center Study to Evaluate the Persistence Of Antibody Responses Among Children Who Previously Received 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	2014-005133-30
Trial protocol	Outside EU/EEA
Global end of trial date	23 April 2013

Results information

Result version number	v2 (current)
This version publication date	01 June 2016
First version publication date	25 April 2015
Version creation reason	• Correction of full data set re-QC of study because of EudraCT system glitch and updates to the results are required.

Trial information

Trial identification

Sponsor protocol code	V59P14E1

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01148017
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Vaccines and Diagnostics
Sponsor organisation address	350 Massachusetts Avenue, Cambridge, United States, 02139
Public contact	Posting Director, Novartis Vaccines & Diagnostics, Inc, RegistryContactVaccinesUS@novartis.com
Scientific contact	Posting Director, Novartis Vaccines & Diagnostics, Inc, 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	09 April 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	23 April 2013
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 in children of 40 and 60 months of age previously vaccinated with MenACWY in study V59P14, as measured by percentage of subjects with human Serum Bactericidal Assay (hSBA) titers 1:8 directed against N. meningitidis serogroups A, C, W-135, and Y.

Protection of trial subjects:

This clinical study was designed, conducted, 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 applicable Standard Operating Procedures (SOPs), with the ethical principles laid down in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 July 2010
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	5 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 433
Worldwide total number of subjects	433
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)	433
Adolescents (12-17 years)	0
Adults (18-64 years)	0

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects who participated at US sites in the V59P14 trial (NCT00474526) were recruited for this extension study, with an aim to reach 400 subjects enrolled. A total of 27 sites in the US participated in the extension study (V59P14E1) at the 40-month timepoint and 18 sites in the US participated at the 60-month timepoint.

Pre-assignment

Screening details:

Priority for enrollment for both the ACWY-4 and ACWY-2 groups was given to those subjects who were part of the primary per protocol (PP) population, followed by subjects with available hSBA result for at least 1 serogroup and then the subjects without any hSBA data available.

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:

Laboratory personnel were blinded so that vaccine groups would not be identifiable during the testing.

Arms

Are arms mutually exclusive?	Yes
Arm title	ACWY - 4

Arm description:

Subjects who had previously received 4 doses of MenACWY-CRM in the parent study during their first year of life, were administered one booster dose of the same vaccine at 60 months 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:

0.5 mL of MenACWY intramuscular (IM) injection in the left deltoid.

Arm title	ACWY - 2

Arm description:

Subjects who had previously received 1 or 2 doses of MenACWY-CRM in the parent study during their second year of life, were administered one booster dose of the same vaccine at 60 months 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:

0.5 mL of MenACWY IM injection in the left deltoid.

Arm title	Naïve - 40

Arm description:

Control subjects, age-matched with the intervention groups subjects (40 months of age), to receive 1

optional dose of MenACWY-CRM.

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:

0.5 mL of MenACWY IM injection in the left deltoid.

Arm title	Naïve - 60

Arm description:

Control subjects, age-matched with the intervention groups subjects (60 months of age), were administered one dose of MenACWY-CRM.

Arm type	Active comparator
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:

0.5 mL of MenACWY IM injection in the left deltoid.

Number of subjects in period 1	ACWY - 4	ACWY - 2	Naïve - 40
Started	214	121	53
Completed	134	87	53
Not completed	80	34	0
Consent withdrawn by subject	31	14	-
Inappropriate enrollment	1	-	-
Unable to classify	3	1	-
Lost to follow-up	23	10	-
Administrative reason	22	9	-

Number of subjects in period 1	Naïve - 60
Started	45
Completed	45
Not completed	0
Consent withdrawn by subject	-
Inappropriate enrollment	-
Unable to classify	-
Lost to follow-up	-
Administrative reason	-

Baseline characteristics

Reporting groups	
Reporting group title	ACWY - 4
Reporting group description:	
Subjects who had previously received 4 doses of MenACWY-CRM in the parent study during their first year of life, were administered one booster dose of the same vaccine at 60 months of age.	
Reporting group title	ACWY - 2
Reporting group description:	
Subjects who had previously received 1 or 2 doses of MenACWY-CRM in the parent study during their second year of life, were administered one booster dose of the same vaccine at 60 months of age.	
Reporting group title	Naïve - 40
Reporting group description:	
Control subjects, age-matched with the intervention groups subjects (40 months of age), to receive 1 optional dose of MenACWY-CRM.	
Reporting group title	Naïve - 60
Reporting group description:	
Control subjects, age-matched with the intervention groups subjects (60 months of age), were administered one dose of MenACWY-CRM.	

Reporting group values	ACWY - 4	ACWY - 2	Naïve - 40
Number of subjects	214	121	53
Age categorical Units: Subjects			
Age continuous Units: months			
arithmetic mean	39.6	39.5	38.7
standard deviation	± 3.4	± 2.4	± 1.8
Gender categorical Units: Subjects			
Female	97	55	29
Male	117	66	24

Reporting group values	Naïve - 60	Total	
Number of subjects	45	433	
Age categorical Units: Subjects			
Age continuous Units: months			
arithmetic mean	60		
standard deviation	± 1.7	-	
Gender categorical Units: Subjects			
Female	26	207	
Male	19	226	

End points

End points reporting groups

Reporting group title	ACWY - 4

Reporting group description:

Subjects who had previously received 4 doses of MenACWY-CRM in the parent study during their first year of life, were administered one booster dose of the same vaccine at 60 months of age.

Reporting group title	ACWY - 2

Reporting group description:

Subjects who had previously received 1 or 2 doses of MenACWY-CRM in the parent study during their second year of life, were administered one booster dose of the same vaccine at 60 months of age.

Reporting group title	Naïve - 40

Reporting group description:

Control subjects, age-matched with the intervention groups subjects (40 months of age), to receive 1 optional dose of MenACWY-CRM.

Reporting group title	Naïve - 60

Reporting group description:

Control subjects, age-matched with the intervention groups subjects (60 months of age), were administered one dose of MenACWY-CRM.

Subject analysis set title	Enrolled Population
Subject analysis set type	Safety analysis

Subject analysis set description:

All subjects who had signed an informed consent, undergone screening procedures, and were enrolled.

Subject analysis set title	PPS 40-Month Persistence
Subject analysis set type	Per protocol

Subject analysis set description:

All subjects in the 40 Month Persistence FAS population who had no major protocol deviation as defined prior to database lock.

Subject analysis set title	PPS 60-Month Persistence
Subject analysis set type	Per protocol

Subject analysis set description:

All subjects in the 60 Month Persistence FAS population who had no major protocol deviation as defined prior to database lock.

Subject analysis set title	PPS Post-MenACWY-CRM
Subject analysis set type	Per protocol

Subject analysis set description:

All subjects in the enrolled population who correctly received the vaccine, provided at least one evaluable serum sample at the relevant time points and whose assay result was available for at least one serogroup with no major protocol deviation.

Subject analysis set title	Safety Solicited AEs from 6 Hour to Day 7
Subject analysis set type	Safety analysis

Subject analysis set description:

All subjects who received a vaccination at 60 months and provided postvaccination solicited safety data.

Subject analysis set title	Post MenACWY at 60 months safety set
Subject analysis set type	Safety analysis

Subject analysis set description:

All subjects who received a vaccination at 60 months and were assessed for postvaccination safety

Primary: Percentages of Subjects With Human Serum Bactericidal Assay (hSBA) Titers ≥ 1:8 Directed Against N. Meningitidis Serogroups A, C, W, and Y at 40 months of age

End point title	Percentages of Subjects With Human Serum Bactericidal Assay (hSBA) Titers ≥ 1:8 Directed Against N. Meningitidis Serogroups A, C, W, and Y at 40 months of age[1][2]

End point description:

The persistence of the antibody response in subjects at 40 months of age, previously vaccinated with two or four doses of MenACWY-CRM in the parent study, and baseline antibody levels in age-matched naive subjects, was measured by the percentage of subjects with human Serum Bactericidal Assay (hSBA) titers ≥ 1:8 directed against N. meningitidis serogroups A, C, W, and Y.
Analysis was done on the 40-month persistence Per Protocol Set (40-month persistence PPS), i.e, all subjects in the enrolled population who provided an evaluable serum sample at the 40-months of age visit and had no major protocol deviations.

End point type	Primary

End point timeframe:

Visit 9 (continuation from the parent study), 40-month visit

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 null hypothesis associated with this immunogenicity objective.

[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: There was no statistical null hypothesis associated with this immunogenicity objective.

End point values	ACWY - 4	ACWY - 2	Naïve - 40	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	206	117	51	
Units: Percentages of subjects				
number (confidence interval 95%)				
Men A	10 (6 to 15)	35 (26 to 44)	2 (0.05 to 10)	
Men C (N=206, 116, 51)	34 (28 to 41)	51 (41 to 60)	12 (4 to 24)	
Men W (N=204, 115, 51)	76 (70 to 82)	83 (74 to 89)	47 (33 to 62)	
Men Y (N=205, 116, 51)	67 (60 to 73)	71 (62 to 79)	22 (11 to 35)	

Statistical analyses

No statistical analyses for this end point

Primary: Percentages of Subjects With Human Serum Bactericidal Assay (hSBA) Titers ≥ 1:8 Directed Against N. Meningitidis Serogroups A, C, W, and Y at 60 months of age

End point title	Percentages of Subjects With Human Serum Bactericidal Assay (hSBA) Titers ≥ 1:8 Directed Against N. Meningitidis Serogroups A, C, W, and Y at 60 months of age[3][4]

End point description:

The persistence of the antibody response in subjects of 60 months of age previously vaccinated with two or four doses of MenACWY-CRM in the parent study, and baseline antibody levels in age-matched naive subjects, was measured by the percentages of subjects with human Serum Bactericidal Assay (hSBA) titers ≥ 1:8 directed against N. meningitidis serogroups A, C, W, and Y.
Analysis was done on the 60-Month persistence Per Protocol Set (60-month persistence PPS), i.e, all subjects in the enrolled population who provided an evaluable serum sample at the 60-months of age visit and had no major protocol deviations.

End point type	Primary

End point timeframe:

Visit 10 (continuation from the parent study), 60 months of age

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: There was no statistical null hypothesis associated with this immunogenicity objective.

[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: There was no statistical null hypothesis associated with this immunogenicity objective.

End point values	ACWY - 4	ACWY - 2	Naïve - 60	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	123	80	45	
Units: Percentages of subjects				
number (confidence interval 95%)				
Men A	6 (2 to 11)	25 (16 to 36)	2 (0.056 to 12)	
Men C	27 (19 to 36)	43 (32 to 54)	22 (11 to 37)	
Men W (N=121, 78, 45)	69 (60 to 77)	74 (63 to 84)	40 (26 to 56)	
Men Y (N=122, 80, 44)	56 (46 to 65)	69 (57 to 79)	25 (13 to 40)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentages of Subjects With hSBA Titers ≥ 1:4 Against N Meningitidis Serogroups A, C, W, and Y at 40 Months of Age

End point title	Percentages of Subjects With hSBA Titers ≥ 1:4 Against N Meningitidis Serogroups A, C, W, and Y at 40 Months of Age[5]

End point description:

The persistence of the antibody response in subjects of 40 months of age previously vaccinated with two or four doses of MenACWY-CRM in the parent study, and baseline antibody levels in age-matched naive subjects, was measured by the percentage of subjects with human Serum Bactericidal Assay (hSBA) titers ≥ 1:4 directed against N. meningitidis serogroups A, C, W, and Y.
Analysis was done on the PPS 40-month persistence.

End point type	Secondary

End point timeframe:

Visit 9 (continuation from the parent study), 40 months of age.

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: There was no statistical null hypothesis associated with this immunogenicity objective.

End point values	ACWY - 4	ACWY - 2	Naïve - 40	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	206	117	51	
Units: Percentages of subjects				
number (confidence interval 95%)				
Men A	13 (9 to 18)	40 (31 to 50)	2 (0.05 to 10)	
Men C (N=206, 116, 51)	43 (36 to 50)	61 (52 to 70)	16 (7 to 29)	
Men W (N=204, 115, 51)	81 (75 to 86)	88 (80 to 93)	49 (35 to 63)	
Men Y (N=205, 116, 51)	76 (69 to 81)	80 (72 to 87)	24 (13 to 37)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentages of Subjects With hSBA Titers ≥ 1:4 Against N Meningitidis Serogroups A, C, W, and Y at 60 Months of Age

End point title	Percentages of Subjects With hSBA Titers ≥ 1:4 Against N Meningitidis Serogroups A, C, W, and Y at 60 Months of Age[6]

End point description:

The persistence of the antibody response in subjects of 60 months of age previously vaccinated with two or four doses of MenACWY-CRM in the parent study, and baseline antibody levels in age-matched naive subjects, was measured by the percentage of subjects with human Serum Bactericidal Assay (hSBA) titers ≥ 1:4 directed against N. meningitidis serogroups A, C, W, and Y.
Analysis was done on the 60-Month persistence PPS.

End point type	Secondary

End point timeframe:

Visit 10 (continuation from the parent study), 60 months of age.

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: There was no statistical null hypothesis associated with this immunogenicity objective.

End point values	ACWY - 4	ACWY - 2	Naïve - 60	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	123	80	45	
Units: Percentages of subjects				
number (confidence interval 95%)				
Men A	9 (5 to 15)	33 (22 to 44)	2 (0.056 to 12)	
Men C	46 (37 to 55)	60 (48 to 71)	33 (20 to 49)	
Men W (N=121, 78, 45)	74 (66 to 82)	83 (73 to 91)	42 (28 to 58)	
Men Y (N=122, 80, 44)	65 (56 to 73)	74 (63 to 83)	25 (13 to 40)	

Statistical analyses

No statistical analyses for this end point

Secondary: hSBA Geometric Mean Titers (GMTs) Directed Against N. Meningitidis Serogroups A, C, W, and Y at 40 Months of Age

End point title	hSBA Geometric Mean Titers (GMTs) Directed Against N. Meningitidis Serogroups A, C, W, and Y at 40 Months of Age[7]

End point description:

The persistence of the antibody response in children of 40 months of age previously vaccinated with two or four doses of MenACWY-CRM in study V59P14, and baseline antibody levels in age-matched naive subjects, was measured by the hSBA GMTs directed against N meningitidis serogroups A, C, W, and Y.
Analysis was done on the 40-month persistence PPS.

End point type	Secondary

End point timeframe:

Visit 9 (continuation from the parent study), 40-months of age.

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: There was no statistical null hypothesis associated with this immunogenicity objective.

End point values	ACWY - 4	ACWY - 2	Naïve - 40	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	206	117	51	
Units: Titers				
geometric mean (confidence interval 95%)				
Men A	2.54 (2.23 to 2.9)	4.81 (4.06 to 5.69)	2.02 (1.57 to 2.61)	
Men C (N=206, 116, 51)	6.14 (4.98 to 7.59)	9.24 (7.05 to 12)	2.52 (1.68 to 3.78)	
Men W (N=204, 115, 51)	26 (21 to 32)	29 (22 to 39)	8.25 (5.47 to 12)	
Men Y (N=205, 116, 51)	16 (13 to 20)	18 (14 to 24)	3.69 (2.44 to 5.57)	

Statistical analyses

No statistical analyses for this end point

Secondary: hSBA GMTs Directed Against N Meningitidis Serogroups A, C, W, and Y at 60 Months of Age

End point title	hSBA GMTs Directed Against N Meningitidis Serogroups A, C, W, and Y at 60 Months of Age[8]

End point description:

The persistence of the antibody response in children of 60 months of age previously vaccinated with two or four doses of MenACWY-CRM in study V59P14, and baseline antibody levels in age-matched naive subjects was measured by the hSBA GMTs directed against N meningitidis serogroups A, C, W, and Y.

End point type	Secondary

End point timeframe:

Visit 10 (continuation from the parent study), 60 months of age.

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: There was no statistical null hypothesis associated with this immunogenicity objective.

End point values	ACWY - 4	ACWY - 2	Naïve - 60	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	123	80	45	
Units: Titers				
geometric mean (confidence interval 95%)				
Men A	2.27 (1.95 to 2.63)	3.74 (3.12 to 4.48)	2.14 (1.68 to 2.74)	
Men C	5.17 (3.96 to 6.75)	9.26 (6.71 to 13)	3.87 (2.5 to 5.98)	

Men W (N=121, 78, 45)	17 (13 to 22)	20 (14 to 28)	6.63 (4.25 to 10)	
Men Y (N=122, 80, 44)	11 (8.1 to 14)	14 (9.94 to 19)	4.1 (2.61 to 6.45)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentages of Subjects With hSBA Titers ≥ 1:8, and ≥ 1:4 Directed Against N. Meningitidis Serogroups A, C, W, and Y, at 1 Month Post-vaccination with MenACWY-CRM at 60 months of age

End point title	Percentages of Subjects With hSBA Titers ≥ 1:8, and ≥ 1:4 Directed Against N. Meningitidis Serogroups A, C, W, and Y, at 1 Month Post-vaccination with MenACWY-CRM at 60 months of age[9]

End point description:

The antibody response to one booster dose of MenACWY-CRM in children of 60 months of age who had previously received at least one dose of MenACWY-CRM in the parent study compared to the antibody response to one dose of MenACWY-CRM in meningococcal vaccine-naïve subjects, was measured by the percentage of subjects with hSBA titers ≥ 1:8 and ≥1:4 directed against N. meningitidis serogroups A, C, W, and Y, at 1 month post-vaccination.
Analysis was done on the PPS-Immunogenicity after one dose of MenACWY-CRM.

End point type	Secondary

End point timeframe:

Visit 11, 1 month after vaccination.

Notes:

[9] - 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: There was no statistical null hypothesis associated with this immunogenicity objective.

End point values	ACWY - 4	ACWY - 2	Naïve - 60	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	116	76	45	
Units: Percentages of subjects				
number (confidence interval 95%)				
Men A (≥1:8)	97 (91 to 99)	97 (91 to 100)	87 (73 to 95)	
Men C (≥1:8; N=115, 75, 45)	96 (90 to 99)	99 (93 to 100)	84 (71 to 94)	
Men W (≥1:8; N=104, 70, 44)	100 (97 to 100)	100 (95 to 100)	89 (75 to 96)	
Men Y (≥1:8; N=111, 74, 44)	100 (97 to 100)	100 (95 to 100)	73 (57 to 85)	
Men A (≥1:4)	97 (91 to 99)	97 (91 to 100)	89 (76 to 96)	
Men C (≥1:4; N=115, 75, 45)	97 (93 to 99)	100 (95 to 100)	87 (73 to 95)	
Men W (≥1:4; N=104, 70, 44)	100 (97 to 100)	100 (95 to 100)	91 (78 to 97)	
Men Y (≥1:4; N=111, 74, 44)	100 (97 to 100)	100 (95 to 100)	80 (65 to 90)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Seroresponse at 1 Month Post-vaccination

End point title	Percentage of Subjects With Seroresponse at 1 Month Post-vaccination[10]

End point description:

The antibody response to one booster dose of MenACWY-CRM in children of 60 months of age who had previously received at least one dose of MenACWY-CRM in the parent study, compared to the antibody response to one dose of MenACWY-CRM in meningococcal vaccine-naïve subjects, was measured by the percentage of subjects with seroresponse at 1 month post-vaccination.
Analysis was done on the PPS Post-MenACWY-CRM.

End point type	Secondary

End point timeframe:

Visit 11, 1 month after vaccination.

Notes:

[10] - 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: There was no statistical null hypothesis associated with this immunogenicity objective.

End point values	ACWY - 4	ACWY - 2	Naïve - 60	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	116	76	45	
Units: Percentages of subjects				
number (confidence interval 95%)				
Men A	97 (91 to 99)	96 (89 to 99)	87 (73 to 95)	
Men C (N=115, 75, 45)	87 (79 to 93)	87 (77 to 93)	73 (58 to 85)	
Men W (N=104, 70, 44)	99 (95 to 100)	100 (95 to 100)	57 (41 to 72)	
Men Y (N=111, 74, 44)	98 (94 to 100)	99 (93 to 100)	52 (37 to 68)	

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of Subjects Reporting Solicited Local and Systemic Adverse Events (AEs) and Other Indicators of Reactogenicity[11]

End point description:

Number of subjects reporting solicited local and systemic Adverse Events (AEs) and other indicators of reactogenicity after receiving study vaccination.
Note: Solicited AEs were not recorded for naive subjects at 40 months of age, but only SAEs and medically attended AEs.
Analysis was done on the Solicited Safety Set (from 6 hours to day 7)

End point type	Secondary

End point timeframe:

From day 1 to 7 after vaccination.

Notes:

[11] - 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: There was no statistical null hypothesis associated with this immunogenicity objective.

End point values	ACWY - 4	ACWY - 2	Naïve - 60	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	129	83	45[12]	
Units: Percentages of subjects				
number (not applicable)				
Any local	67	44	29	
Injection site pain	54	33	24	
Injection site erythema	26	20	13	
Injection site induration	18	14	10	
Any systemic	45	26	23	
Change in eating habits	14	5	4	
Sleepiness	20	9	7	
Irritability	24	14	8	
Vomiting	4	0	3	
Diarrhea	7	1	1	
Arthralgia	2	4	0	
Headache	6	6	2	
Rash	4	2	3	
Fever	4	2	2	
Any other	18	11	7	
Stayed home due to reaction	5	0	0	
Use of analgesics/antipyretics	18	11	7	

Notes:

[12] - Actual number of subjects analyzed was 49.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentages of Subjects Reporting Unsolicited AEs and SAEs

End point title	Percentages of Subjects Reporting Unsolicited AEs and SAEs

End point description:

Percentages of subjects reporting unsolicited AEs, serious adverse events (SAEs) and medically attended AEs after receiving study vaccination.
Analysis was done on the Post MenACWY at 40 and 60 months safety set

End point type	Secondary

End point timeframe:

Day 1 to 7 after vaccination for any unsolicited AEs, day 1 to study termination for SAEs and medically attended AEs (for the naive-40 group), day 8 to study termination for SAEs and medically attended AEs (for the other groups).

End point values	ACWY - 4	ACWY - 2	Naïve - 40	Naïve - 60
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	132	87	11[13]	45[14]
Units: Percentages of subjects				
Any unsolicited AE	7	8	0	12
Possibly related AE	4	6	0	6
Medically attended AEs	0	0	27	0
Any SAE	0	0	0	0

Notes:

[13] - Unsolicated AEs were not recorded for this group

[14] - Actual number of subjects analyzed was 50.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited and unsolicited AEs were collected from day 1 to day 7 after vaccination. Serious AEs were collected from day 1 to study termination.

Adverse event reporting additional description:

Analysis for the solicited and unsolicited non-serious AEs was done on the Overall Post MenACWY Safety Set, ie, all subjects who received a vaccination at 40 or 60 months and were assessed for postvaccination safety. Analysis for serious adverse events was done on the Post MenACWY at 60 Months and at 40 Months Safety Sets.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	15.0

Reporting groups

Reporting group title	ACWY - 4

Reporting group description:

Subjects who previously received 4 doses of MenACWY-CRM in the parent study during their first year of life, were administered one booster dose of the same vaccine at 60 months of age.

Reporting group title	ACWY - 2

Reporting group description:

Subjects who previously received 1 or 2 doses of MenACWY-CRM in the parent study during their second year of life, were administered one booster dose of the same vaccine at 60 months of age.

Reporting group title	Naïve - 40

Reporting group description:

Control subjects, age-matched with the intervention groups subjects (40 months of age), to receive 1 optional dose of MenACWY-CRM.

Reporting group title	Naïve - 60

Reporting group description:

Control subjects, age-matched with the intervention groups subjects (60 months of age), were administered one dose of MenACWY-CRM.

Serious adverse events	ACWY - 4	ACWY - 2	Naïve - 40
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 132 (0.00%)	0 / 87 (0.00%)	0 / 11 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	Naïve - 60		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 50 (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	ACWY - 4	ACWY - 2	Naïve - 40
Total subjects affected by non-serious adverse events			
subjects affected / exposed	87 / 132 (65.91%)	57 / 87 (65.52%)	3 / 11 (27.27%)
Nervous system disorders			
Headache			
subjects affected / exposed	6 / 132 (4.55%)	7 / 87 (8.05%)	0 / 11 (0.00%)
occurrences (all)	6	9	0
Somnolence			
subjects affected / exposed	21 / 132 (15.91%)	9 / 87 (10.34%)	0 / 11 (0.00%)
occurrences (all)	25	9	0
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	26 / 132 (19.70%)	22 / 87 (25.29%)	0 / 11 (0.00%)
occurrences (all)	26	23	0
Injection site induration			
subjects affected / exposed	21 / 132 (15.91%)	15 / 87 (17.24%)	0 / 11 (0.00%)
occurrences (all)	22	16	0
Injection site pain			
subjects affected / exposed	59 / 132 (44.70%)	37 / 87 (42.53%)	0 / 11 (0.00%)
occurrences (all)	60	38	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	7 / 132 (5.30%)	2 / 87 (2.30%)	0 / 11 (0.00%)
occurrences (all)	8	3	0
Vomiting			
subjects affected / exposed	4 / 132 (3.03%)	0 / 87 (0.00%)	0 / 11 (0.00%)
occurrences (all)	4	0	0
Skin and subcutaneous tissue disorders			
Ingrowing nail			
subjects affected / exposed	0 / 132 (0.00%)	0 / 87 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1

Rash			
subjects affected / exposed	4 / 132 (3.03%)	2 / 87 (2.30%)	0 / 11 (0.00%)
occurrences (all)	4	2	0
Psychiatric disorders			
Irritability			
subjects affected / exposed	24 / 132 (18.18%)	14 / 87 (16.09%)	0 / 11 (0.00%)
occurrences (all)	27	15	0
Eating disorders			
subjects affected / exposed	14 / 132 (10.61%)	5 / 87 (5.75%)	0 / 11 (0.00%)
occurrences (all)	17	5	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 132 (1.52%)	4 / 87 (4.60%)	1 / 11 (9.09%)
occurrences (all)	2	5	1
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	0 / 132 (0.00%)	1 / 87 (1.15%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Otitis media acute			
subjects affected / exposed	1 / 132 (0.76%)	0 / 87 (0.00%)	1 / 11 (9.09%)
occurrences (all)	1	0	1
Upper respiratory tract infection			
subjects affected / exposed	0 / 132 (0.00%)	0 / 87 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Viral pharyngitis			
subjects affected / exposed	0 / 132 (0.00%)	0 / 87 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1

Non-serious adverse events	Naïve - 60		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	39 / 50 (78.00%)		
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 50 (4.00%)		
occurrences (all)	2		
Somnolence			

subjects affected / exposed	7 / 50 (14.00%)		
occurrences (all)	7		
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	13 / 50 (26.00%)		
occurrences (all)	13		
Injection site induration			
subjects affected / exposed	11 / 50 (22.00%)		
occurrences (all)	12		
Injection site pain			
subjects affected / exposed	24 / 50 (48.00%)		
occurrences (all)	25		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 50 (2.00%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	3 / 50 (6.00%)		
occurrences (all)	3		
Skin and subcutaneous tissue disorders			
Ingrowing nail			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences (all)	0		
Rash			
subjects affected / exposed	3 / 50 (6.00%)		
occurrences (all)	3		
Psychiatric disorders			
Irritability			
subjects affected / exposed	9 / 50 (18.00%)		
occurrences (all)	9		
Eating disorders			
subjects affected / exposed	4 / 50 (8.00%)		
occurrences (all)	4		
Musculoskeletal and connective tissue disorders			
Arthralgia			

subjects affected / exposed	1 / 50 (2.00%)		
occurrences (all)	1		
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	4 / 50 (8.00%)		
occurrences (all)	4		
Otitis media acute			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences (all)	0		
Upper respiratory tract infection			
subjects affected / exposed	2 / 50 (4.00%)		
occurrences (all)	2		
Viral pharyngitis			
subjects affected / exposed	0 / 50 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported