Clinical trial results:
A Phase IIIb, Open-Label, Controlled, Multi-Center Study to Evaluate the Persistence Of Antibody Responses Among Children Who Previously Received Novartis MenACWY Conjugate Vaccine or Meningococcal C Conjugate Vaccine

Summary

EudraCT number	2010-023858-37
Trial protocol	DE
Global end of trial date	08 September 2011

Results information

Result version number	v2 (current)
This version publication date	11 May 2016
First version publication date	28 December 2014
Version creation reason	• Correction of full data set Data points need to be updated.

Trial information

Trial identification

Sponsor protocol code	V59P22E1

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01345721
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 and Diagnostics S.r.l., RegistryContactVaccinesUS@novartis.com
Scientific contact	Posting Director, Novartis Vaccines and Diagnostics S.r.l., 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	03 May 2012
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	08 September 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Co-primary objectives:
1.To evaluate the persistence of the antibody response in children previously vaccinated with one or two doses of MenACWY or MenC in study V59P22, as measured by percentage of subjects with human Serum Bactericidal Assay (hSBA) titers ≥ 1:8 directed against N. meningitidis serogroups A, C, W and Y.
2.To evaluate the antibody response to a booster dose of MenACWY in children previously vaccinated with one or two doses of MenACWY as measured by of percentage of subjects with hSBA titers ≥ 1:8, and hSBA GMTs directed against N.meningitidis serogroups A, C, W, Y.
3.To evaluate the antibody response to one dose of MenACWY in children previously vaccinated with MenC as measured by of percentage of subjects with hSBA titers ≥ 1:8, and hSBA GMTs directed against N. meningitidis serogroups A, C, W, Y.

Protection of trial subjects:

Study vaccines were not administered to individuals with known hypersensitivity to any component of the vaccines. An oral temperature ≥38.0°C (≥100.4°F) or serious active infection was a reason for delaying vaccination. 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 is not injected into a blood vessel.

Background therapy:

MenACWY

Evidence for comparator:

MenC

Actual start date of recruitment	25 May 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	Germany: 205
Worldwide total number of subjects	205
EEA total number of subjects	205

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)	205
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 for this extension study were enrolled between 25 May 2011 and 08 September 2011 from only sites in Germany that participated in the parent study.

Pre-assignment

Screening details:

Subjects were 22 to 45 months of age at the time of enrolment into V59P22E1 and had participated in the original V59P22 study.

Period 1

Period 1 title	overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	MenACWY_2 doses + MenACWY booster

Arm description:

Subjects, who had received two doses of MenACWY (at 6 to 8 months and 12 months of age) in the parent study, were administered a booster dose of MenACWY at 22 to 45 months of age in this extension study.

Arm type	Experimental
Investigational medicinal product name	MenACWY-CRM
Investigational medicinal product code	
Other name	Meningococcal (groups A, C, Y, and W-135 vaccine) Oligosaccharide Diptheria-CRM197 Conjugate Vaccine
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

MenACWY was obtained by extemporaneous mixing just before injection of the lyophilized MenA component with the liquid MenCWY component. One 0.5 mL dose of MenACWY was administered by IM injection in the left deltoid.

Arm title	MenACWY_1 dose + MenACWY booster

Arm description:

Subjects, who had received one dose of MenACWY (at 12 months of age) in the parent study, were administered a booster dose of MenACWY at 22 to 45 months of age in this extension study.

Arm type	Experimental
Investigational medicinal product name	MenACWY-CRM
Investigational medicinal product code	
Other name	Meningococcal (groups A, C, Y, and W-135 vaccine) Oligosaccharide Diptheria-CRM197 Conjugate Vaccine
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

MenACWY was obtained by extemporaneous mixing just before injection of the lyophilized MenA component with the liquid MenCWY component. One 0.5 mL dose of MenACWY was administered by IM injection in the left deltoid.

Arm title	Men C + MenACWY booster

Arm description:

Subjects, who had received one dose of the comparator MenC vaccine (at 12 months of age) in the parent study, were administered a booster dose of MenACWY at 22 to 45 months of age in this extension study.

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:

MenACWY was obtained by extemporaneous mixing just before injection of the lyophilized MenA component with the liquid MenCWY component. One 0.5 mL dose of MenACWY was administered by IM injection in the left deltoid.

Number of subjects in period 1	MenACWY_2 doses + MenACWY booster	MenACWY_1 dose + MenACWY booster	Men C + MenACWY booster
Started	74	66	65
Completed	74	66	65

Baseline characteristics

Reporting groups	
Reporting group title	MenACWY_2 doses + MenACWY booster
Reporting group description:	
Subjects, who had received two doses of MenACWY (at 6 to 8 months and 12 months of age) in the parent study, were administered a booster dose of MenACWY at 22 to 45 months of age in this extension study.	
Reporting group title	MenACWY_1 dose + MenACWY booster
Reporting group description:	
Subjects, who had received one dose of MenACWY (at 12 months of age) in the parent study, were administered a booster dose of MenACWY at 22 to 45 months of age in this extension study.	
Reporting group title	Men C + MenACWY booster
Reporting group description:	
Subjects, who had received one dose of the comparator MenC vaccine (at 12 months of age) in the parent study, were administered a booster dose of MenACWY at 22 to 45 months of age in this extension study.	

Reporting group values	MenACWY_2 doses + MenACWY booster	MenACWY_1 dose + MenACWY booster	Men C + MenACWY booster
Number of subjects	74	66	65
Age categorical Units: Subjects			
Children (2-11 years)	74	66	65
Age continuous Units: months			
arithmetic mean	36.7	37.4	37.9
standard deviation	± 5.3	± 5.6	± 5.3
Gender categorical Units: Subjects			
Female	34	30	37
Male	40	36	28

Reporting group values	Total		
Number of subjects	205		
Age categorical Units: Subjects			
Children (2-11 years)	205		
Age continuous Units: months			
arithmetic mean			
standard deviation	-		
Gender categorical Units: Subjects			
Female	101		
Male	104		

Subject analysis sets

Subject analysis set title	Per Protocol Persistence Population
Subject analysis set type	Per protocol

Subject analysis set description:

All subjects who provided evaluable serum samples at visit 7 and had no major protocol violation as defined prior to the end of the study

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

Subject analysis set description:

All subjects in the Exposed population who received at least one dose of study vaccine, and provided some post-vaccination safety data

Subject analysis set title	Per-protocol Population
Subject analysis set type	Per protocol

Subject analysis set description:

All enrolled subjects who correctly received the vaccine, provided evaluable serum samples at the relevant time points (Day 28), and had no
major protocol violation as defined prior to the end of the study.

Reporting group values	Per Protocol Persistence Population	Safety Population	Per-protocol Population
Number of subjects	136	140	134
Age categorical Units: Subjects			
Children (2-11 years)	136	140	134
Age continuous Units: months arithmetic mean standard deviation	±	±	±
Gender categorical Units: Subjects			
Female Male			

End points

End points reporting groups

Reporting group title	MenACWY_2 doses + MenACWY booster
Reporting group description:	
Subjects, who had received two doses of MenACWY (at 6 to 8 months and 12 months of age) in the parent study, were administered a booster dose of MenACWY at 22 to 45 months of age in this extension study.	
Reporting group title	MenACWY_1 dose + MenACWY booster
Reporting group description:	
Subjects, who had received one dose of MenACWY (at 12 months of age) in the parent study, were administered a booster dose of MenACWY at 22 to 45 months of age in this extension study.	
Reporting group title	Men C + MenACWY booster
Reporting group description:	
Subjects, who had received one dose of the comparator MenC vaccine (at 12 months of age) in the parent study, were administered a booster dose of MenACWY at 22 to 45 months of age in this extension study.	
Subject analysis set title	Per Protocol Persistence Population
Subject analysis set type	Per protocol
Subject analysis set description:	
All subjects who provided evaluable serum samples at visit 7 and had no major protocol violation as defined prior to the end of the study	
Subject analysis set title	Safety Population
Subject analysis set type	Safety analysis
Subject analysis set description:	
All subjects in the Exposed population who received at least one dose of study vaccine, and provided some post-vaccination safety data	
Subject analysis set title	Per-protocol Population
Subject analysis set type	Per protocol
Subject analysis set description:	
All enrolled subjects who correctly received the vaccine, provided evaluable serum samples at the relevant time points (Day 28), and had no major protocol violation as defined prior to the end of the study.	

Primary: Percentage of Subjects With Persisting Serum Bactericidal Antibody Titers ≥ 1:8, Upto 13-33 Months After Primary Vaccination With Either MenACWY-CRM or MenC Vaccine

End point title	Percentage of Subjects With Persisting Serum Bactericidal Antibody Titers ≥ 1:8, Upto 13-33 Months After Primary Vaccination With Either MenACWY-CRM or MenC Vaccine[1]
End point description:	
The percentage of subjects with persisting serum bactericidal antibody (hSBA) titers ≥ 1:8 against Neisseria meningitidis serogroups A,C,W,Y, 13-33 months after receiving either one or two doses of MenACWY-CRM conjugate vaccine or one dose of MenC vaccine in parent study, is reported. The functional bactericidal antibodies response against N. meningitidis serogroups was measured with the serum bactericidal assay using human complement (hSBA). The analysis was done on the per-protocol persistence population.	
End point type	Primary
End point timeframe:	
13-33 months post-primary 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 analyses were associated with this end point

End point values	MenACWY_2 doses + MenACWY booster	MenACWY_1 dose + MenACWY booster	Men C + MenACWY booster	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	52	41	43	
Units: Percentage of Subjects				
number (confidence interval 95%)				
13-33 months persistence (Serogroup A)	13 (6 to 26)	7 (2 to 20)	0 (0 to 8)	
13-33 months persistence (Serogroup C)(N=52,40,42)	27 (16 to 41)	25 (13 to 41)	36 (22 to 52)	
13-33 months persistence (Serogroup W-135)	50 (36 to 64)	63 (47 to 78)	12 (4 to 25)	
13-33 months persistence (Serogroup Y)	40 (27 to 55)	39 (24 to 55)	19 (8 to 33)	

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Serum Bactericidal Antibody Titers ≥ 1:8, One Month After MenACWY-CRM Booster Vaccination

End point title	Percentage of Subjects With Serum Bactericidal Antibody Titers ≥ 1:8, One Month After MenACWY-CRM Booster Vaccination[2][3]

End point description:

The serum antibody response following a booster dose of MenACWY-CRM conjugate vaccine in children, who had previously received either one or two doses of the same vaccine in the parent study, is reported as percentage of subjects with hSBA titers ≥ 1:8 against N. meningitidis serogroups A,C,W,Y. The analysis was performed on the per-protocol population.

End point type	Primary

End point timeframe:

1 month post-booster vaccination

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses were associated with this end point

[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: As per the objective [MenACWY_2 doses + MenACWY booster] and [MenACWY_1 dose + MenACWY booster] groups were analysed for this outcome measure.

End point values	MenACWY_2 doses + MenACWY booster	MenACWY_1 dose + MenACWY booster		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	41		
Units: Percentage of Subjects				
number (confidence interval 95%)				
Pre-booster (Serogroup A)	13 (6 to 26)	7 (2 to 20)		
1 month post booster (Serogroup A)	96 (87 to 100)	98 (87 to 100)		
Pre-booster (Serogroup C) N=52,40	27 (16 to 41)	25 (13 to 41)		
1 month post booster (Serogroup C) N=52,40	100 (93 to 100)	100 (91 to 100)		

Pre-booster (Serogroup W-135)	50 (36 to 64)	63 (47 to 78)		
1 month post booster (Serogroup W-135)	100 (93 to 100)	100 (91 to 100)		
Pre-booster (Serogroup Y)	40 (27 to 55)	39 (24 to 55)		
1 month post booster (Serogroup Y)	100 (93 to 100)	100 (91 to 100)		

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Titers in Children, One Month After MenACWY-CRM Booster Vaccination

End point title	Geometric Mean Titers in Children, One Month After MenACWY-CRM Booster Vaccination[4][5]

End point description:

The serum antibody titers following a booster dose of MenACWY-CRM conjugate vaccine in children, who had previously received either one or two doses of the same vaccine in the parent study, are reported as geometric mean titers (GMTs) against N. meningitidis serogroups A,C, W,Y.
The analysis was performed on the per-protocol population.

End point type	Primary

End point timeframe:

1 month post-booster vaccination

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses were associated with this end point

[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: As per the objective [MenACWY_2 doses + MenACWY booster] and [MenACWY_1 dose + MenACWY booster] groups were analysed for this outcome measure.

End point values	MenACWY_2 doses + MenACWY booster	MenACWY_1 dose + MenACWY booster		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	41		
Units: Titers				
geometric mean (confidence interval 95%)				
Pre-booster (Serogroup A)	2.82 (2.35 to 3.38)	2.52 (2.05 to 3.09)		
1 month post booster (Serogroup A)	182 (118 to 281)	214 (131 to 350)		
Pre-booster (Serogroup C) N=52,40	3.92 (2.92 to 5.26)	3.91 (2.79 to 5.48)		
1 month post booster (Serogroup C) N=52,40	541 (399 to 733)	968 (682 to 1372)		
Pre-booster (Serogroup W-135)	9.37 (6.3 to 14)	12 (7.51 to 18)		
1 month post booster (Serogroup W-135)	799 (564 to 1133)	1267 (854 to 1879)		
Pre-booster (Serogroup Y)	6.79 (4.86 to 9.5)	6.04 (4.13 to 8.82)		

1 month post booster (Serogroup Y)	650 (448 to 941)	676 (444 to 1027)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects (Who Had Previously Received MenC Vaccine) With Serum Bactericidal Antibody Titers ≥ 1:8, After One Dose of MenACWY-CRM Vaccination

End point title	Percentage of Subjects (Who Had Previously Received MenC Vaccine) With Serum Bactericidal Antibody Titers ≥ 1:8, After One Dose of MenACWY-CRM Vaccination[6][7]

End point description:

The serum antibody response following a dose of MenACWY-CRM conjugate vaccine in children, who had previously received one dose of MenC vaccine in the parent study, is reported as percentage of subjects with hSBA titers ≥1:8 against N. meningitidis serogroups A,C, W,Y.
The analysis was performed on the per-protocol population.

End point type	Primary

End point timeframe:

1 month after vaccination

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses were associated with this end point

[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: As per the objective [Men C + MenACWY booster] group was analysed for this outcome measure.

End point values	Men C + MenACWY booster			
Subject group type	Reporting group			
Number of subjects analysed	41			
Units: Percentage of subjects				
number (confidence interval 95%)				
Prevaccination (Serogroup A)	0 (0 to 9)			
1 month post vaccination (Serogroup A)	61 (45 to 76)			
Prevaccination (Serogroup C) N=39	36 (21 to 53)			
1 month post vaccination (Serogroup C) N=39	100 (91 to 100)			
Pre-booster (Serogroup W-135)	12 (4 to 26)			
1 month post vaccination (Serogroup W-135)	95 (83 to 99)			
Pre- vaccination (Serogroup Y)	20 (9 to 35)			
1 month post vaccination (Serogroup Y)	95 (83 to 99)			

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Titers in Children (Who Previously Received MenC Vaccine) One Month After One Dose of MenACWY-CRM Vaccine

End point title	Geometric Mean Titers in Children (Who Previously Received MenC Vaccine) One Month After One Dose of MenACWY-CRM Vaccine[8][9]

End point description:

The serum antibody titers following one dose of MenACWY-CRM conjugate vaccine in children, who had previously received one dose of MenC vaccine in the parent study, are reported as GMTs against N. meningitidis serogroups A,C,W,Y.
The analysis was performed on the per-protocol population.

End point type	Primary

End point timeframe:

1 month post vaccination

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses were associated with this end point

[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: As per the objective [Men C + MenACWY booster] group was analysed for this outcome measure.

End point values	Men C + MenACWY booster			
Subject group type	Reporting group			
Number of subjects analysed	41			
Units: Titers				
geometric mean (confidence interval 95%)				
Prevaccination (Serogroup A)	2 (1.63 to 2.45)			
1 month post vaccination (Serogroup A)	20 (12 to 32)			
Prevaccination (Serogroup C) N=39	4.83 (3.44 to 6.77)			
1 month post vaccination (Serogroup C) N=39	1530 (1077 to 2173)			
Pre-booster (Serogroup W-135)	2.82 (1.81 to 4.39)			
1 month post vaccination (Serogroup W-135)	54 (37 to 80)			
Pre- vaccination (Serogroup Y)	3.05 (2.09 to 4.44)			
1 month post vaccination (Serogroup Y)	54 (35 to 81)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Children Reporting Solicited Local and Systemic Adverse Events (AEs) After MenACWY-CRM Vaccination

End point title	Number of Children Reporting Solicited Local and Systemic Adverse Events (AEs) After MenACWY-CRM Vaccination

End point description:

The safety of MenACWY-CRM vaccine in children (who had previously received either one or two doses of MenACWY-CRM vaccine or one dose of MenC vaccine in the parent study) is assessed in terms of number of subjects reporting any unsolicited AEs (day 1 to day 7); serious AEs and AEs necessitating medical attention/or premature withdrawal (day 1 to day 28) after MenACWY-CRM vaccine.
The analysis was performed on the safety population.

End point type	Secondary

End point timeframe:

Day 1 to 7 after vaccination

End point values	MenACWY_2 doses + MenACWY booster	MenACWY_1 dose + MenACWY booster	Men C + MenACWY booster	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	53	44	43	
Units: Subjects				
Any Solicited Local	33	30	30	
Pain	10	15	13	
Erythema	14	17	15	
Induration	6	8	7	
Any Solicited Systemic	28	18	25	
Arthralgia	1	5	4	
Headache	5	6	1	
Vomiting	0	2	1	
Change in Eating Habits	6	8	6	
Rash	0	2	1	
Sleepiness	10	13	10	
Fever	8	7	7	
Any other	5	7	5	
Stayed at home	4	5	2	
Analgesic Antipyretic Medication Used	4	6	5	
Temperature (≥40°C) (N= 52,41,41)	0	0	2	

Statistical analyses

No statistical analyses for this end point

Secondary: Persisting Geometric Mean Titers in Children, 13-33 Months After Primary Vaccination With Either MenACWY-CRM or MenC Vaccine

End point title	Persisting Geometric Mean Titers in Children, 13-33 Months After Primary Vaccination With Either MenACWY-CRM or MenC Vaccine

End point description:

The persisting serum bactericidal antibody titers in children, 13-33 months after receiving either one or two doses of MenACWY-CRM vaccine or one dose of Men C vaccine in the parent study, are reported as GMTs against N. meningitidis serogroups A,C, W,Y.
The analysis was performed on the per-protocol persistence population.

End point type	Secondary

End point timeframe:

13-33 months after primary vaccination

End point values	MenACWY_2 doses + MenACWY booster	MenACWY_1 dose + MenACWY booster	Men C + MenACWY booster	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	52	41	43	
Units: Titers				
geometric mean (confidence interval 95%)				
13-33 months persistence (Serogroup A)	2.82 (2.36 to 3.37)	2.52 (2.05 to 3.08)	2 (1.64 to 2.43)	
13-33 months persistence (Serogroup C)(N=52,40)	3.94 (2.92 to 5.3)	3.93 (2.79 to 5.53)	4.94 (3.55 to 6.86)	
13-33 months persistence (Serogroup W-135)	9.36 (6.31 to 14)	12 (7.53 to 18)	2.81 (1.82 to 4.32)	
13-33 months persistence (Serogroup Y)	6.79 (4.87 to 9.47)	6.03 (4.14 to 8.78)	2.99 (2.08 to 4.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Serum Bactericidal Titers ≥1:8, Who Previously Received 1 Primary Dose of Either MenACWY-CRM or Men C Vaccine

End point title	Percentage of Subjects With Serum Bactericidal Titers ≥1:8, Who Previously Received 1 Primary Dose of Either MenACWY-CRM or Men C Vaccine[10]

End point description:

Comparison of serum antibody responses following one dose of MenACWY-CRM conjugate vaccine in children, who had previously received either one dose of the same vaccine or one dose of Men C vaccine in the parent study, is reported as percentage of subjects with hSBA titers ≥1:8 against N. meningitidis serogroups A,C,W,Y.
The analysis was performed on the per-protocol population.

End point type	Secondary

End point timeframe:

1 month post 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: As per the objective [MenACWY_1 dose + MenACWY booster] and [Men C + MenACWY booster] groups were analysed for this outcome measure.

End point values	MenACWY_1 dose + MenACWY booster	Men C + MenACWY booster		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	41		
Units: Percentage of subjects				
number (confidence interval 95%)				
hSBA ≥1:8(Serogroup A)	98 (87 to 100)	61 (45 to 76)		
hSBA ≥1:8 (Serogroup C) N=40,39	100 (91 to 100)	100 (91 to 100)		
hSBA ≥1:8(Serogroup W- 135)	100 (91 to 100)	95 (83 to 99)		
hSBA ≥1:8 (Serogroup Y)	100 (91 to 100)	95 (83 to 99)		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titers Following One Dose of MenACWY-CRM Vaccine in Children Who Previously Received 1 Primary Dose of Either MenACWY-CRM or Men C Vaccine

End point title	Geometric Mean Titers Following One Dose of MenACWY-CRM Vaccine in Children Who Previously Received 1 Primary Dose of Either MenACWY-CRM or Men C Vaccine[11]

End point description:

Comparison of serum antibody titers following a one dose of MenACWY-CRM conjugate vaccine in children, who had previously received either one dose of the same vaccine or one dose of MenC vaccine in the parent study, are reported as GMTs against N. meningitidis serogroups A,C, W,Y.
The analysis was performed on the per-protocol population.

End point type	Secondary

End point timeframe:

1 month post 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: As per the objective [MenACWY_1 dose + MenACWY booster] and [Men C + MenACWY booster] groups were analysed for this outcome measure.

End point values	MenACWY_1 dose + MenACWY booster	Men C + MenACWY booster		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	41		
Units: Titers				
geometric mean (confidence interval 95%)				
1 month post vaccination (Serogroup A)	214 (131 to 350)	20 (12 to 32)		
1 month post vaccination (Serogroup C) N=40,39	968 (682 to 1372)	1530 (1077 to 2173)		

1 month post vaccination (Serogroup W-135)	1267 (854 to 1879)	54 (37 to 80)		
1 month post vaccination (Serogroup Y)	676 (444 to 1027)	54 (35 to 81)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Children Reporting Unsolicited Adverse Events After MenACWY-CRM Vaccination

End point title	Number of Children Reporting Unsolicited Adverse Events After MenACWY-CRM Vaccination

End point description:

The safety of MenACWY-CRM vaccine in children (who had previously received either one or two doses of MenACWY-CRM vaccine or one dose of MenC vaccine in the parent study) is assessed in terms of number of subjects reporting any unsolicited AEs (day 1 to day 7); serious AEs and AEs necessitating medical attention/or premature withdrawal (day 1 to day 28) after MenACWY-CRM vaccine.
The analysis was performed on the safety population.

End point type	Secondary

End point timeframe:

Day 1-28 after vaccination

End point values	MenACWY_2 doses + MenACWY booster	MenACWY_1 dose + MenACWY booster	Men C + MenACWY booster	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	53	44	43	
Units: Subjects				
Any AE	11	10	9	
At least possibly related AEs	0	2	1	
Serious AE	0	0	0	
AEs leading to premature withdrawal	0	0	0	
Deaths	0	0	0	

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 1-7 after vaccination. SAEs and AEs necessitating medical attention/premature withdrawal were collected from Day 1-28.

Adverse event reporting additional description:

Due to non-compliance with protocol, data from one site was excluded in the parent study and subsequently from this extension study. Thus the numbers of subjects analyzed for safety differ from enrolled population.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	14

Reporting groups

Reporting group title	MenACWY_2 doses + MenACWY booster

Reporting group description:

Subjects, who had previously received two primary doses of MenACWY-CRM vaccine (at 6-8 months and 12 months of age) in parent study, were administered one booster dose of the same vaccine in this extension study.

Reporting group title	MenACWY_1 dose + MenACWY booster

Reporting group description:

Subjects, who had previously received one primary dose of MenACWY-CRM vaccine (at 12 months of age) in parent study, were administered one booster dose of the same vaccine in this extension study.

Reporting group title	Men C + MenACWY booster

Reporting group description:

Subjects, who had previously received one primary dose of the comparator MenC vaccine (at 12 months of age) in parent study, were administered one booster dose MenACWY-CRM vaccine in this extension study.

Serious adverse events	MenACWY_2 doses + MenACWY booster	MenACWY_1 dose + MenACWY booster	Men C + MenACWY booster
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 53 (0.00%)	0 / 44 (0.00%)	0 / 43 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

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

Non-serious adverse events	MenACWY_2 doses + MenACWY booster	MenACWY_1 dose + MenACWY booster	Men C + MenACWY booster
Total subjects affected by non-serious adverse events			
subjects affected / exposed	33 / 53 (62.26%)	31 / 44 (70.45%)	30 / 43 (69.77%)
Nervous system disorders			

Somnolence			
alternative assessment type: Systematic			
subjects affected / exposed	10 / 53 (18.87%)	13 / 44 (29.55%)	10 / 43 (23.26%)
occurrences (all)	11	15	10
Headache			
alternative assessment type: Systematic			
subjects affected / exposed	5 / 53 (9.43%)	6 / 44 (13.64%)	1 / 43 (2.33%)
occurrences (all)	5	6	1
General disorders and administration site conditions			
Pyrexia			
alternative assessment type: Systematic			
subjects affected / exposed	8 / 53 (15.09%)	8 / 44 (18.18%)	7 / 43 (16.28%)
occurrences (all)	11	9	10
Irritability			
subjects affected / exposed	12 / 53 (22.64%)	8 / 44 (18.18%)	14 / 43 (32.56%)
occurrences (all)	13	9	16
Injection site erythema			
alternative assessment type: Systematic			
subjects affected / exposed	14 / 53 (26.42%)	17 / 44 (38.64%)	15 / 43 (34.88%)
occurrences (all)	14	17	15
Injection site induration			
alternative assessment type: Systematic			
subjects affected / exposed	6 / 53 (11.32%)	8 / 44 (18.18%)	7 / 43 (16.28%)
occurrences (all)	6	8	7
Injection site pain			
alternative assessment type: Systematic			
subjects affected / exposed	10 / 53 (18.87%)	15 / 44 (34.09%)	13 / 43 (30.23%)
occurrences (all)	10	16	14
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	4 / 53 (7.55%)	2 / 44 (4.55%)	8 / 43 (18.60%)
occurrences (all)	6	3	9
Psychiatric disorders			
Eating disorder			
alternative assessment type: Systematic			

subjects affected / exposed	6 / 53 (11.32%)	8 / 44 (18.18%)	6 / 43 (13.95%)
occurrences (all)	6	10	7
Musculoskeletal and connective tissue disorders			
Arthralgia			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 53 (1.89%)	5 / 44 (11.36%)	4 / 43 (9.30%)
occurrences (all)	1	5	6

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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

1 site was excluded as not compliant with the protocol requirements for safety reporting,(65 subjects [21 subjects in MenACWY 2-dose group, 22 subjects in MEnACWY 1-dose group and 22 subjects in MenC 1-dose group])

Notes: