Clinical trial results:
A Phase 2, Randomized, Controlled, Observer-Blind, Multi-Center Study Assessing the Safety and Immunogenicity of One Dose of Novartis' Meningococcal ACWY-CRM Vaccine and GlaxoSmithKline Biologicals' Meningococcal ACWY-TT Vaccine in Healthy Toddlers

Due to the EudraCT – Results system being out of service between 31 July 2015 and 12 January 2016, these results have been published in compliance with revised timelines.

Summary

EudraCT number	2013-000862-13
Trial protocol	IT
Global end of trial date	11 October 2014

Results information

Result version number	v1 (current)
This version publication date	18 February 2016
First version publication date	18 February 2016

Trial information

Trial identification

Sponsor protocol code	V59_67

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01994629
WHO universal trial number (UTN)	-
Other trial identifiers	Sample data: Sample data

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	22 July 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	11 October 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the reactogenicity of MenACWY-cross reactive material (CRM) and MenACWY-tetanus toxoid (TT) vaccines, given to healthy toddlers at 12-15 months of age, as measured by the percentage of subjects with at least one severe solicited Adverse Event (AE) reported between 6 hours and Day 7 post vaccination.

Protection of trial subjects:

This clinical study was designed and was to be implemented and reported in accordance with the International Conference on Harmonization (ICH) Harmonized Tripartite Guidelines for Good Clinical Practices (GCPs), with applicable local regulations including European Directive 2001/20/EC, United States (US) Code of Federal Regulations Title 21, and Japanese Ministry of Health, Labor, and Welfare, Novartis codes on protection of human rights, and with the ethical principles laid down in the Declaration of Helsinki (European Council 2001, US Code of Federal Regulations, ICH 1997).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 November 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	Italy: 202
Worldwide total number of subjects	202
EEA total number of subjects	202

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)	202
Children (2-11 years)	0
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 were enrolled from 4 centers in Italy.

Pre-assignment

Screening details:

All enrolled subjects were included in the trial.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	MenACWY-CRM (12 to 15 months old)

Arm description:

Subjects received one dose of investigational MenACWY-CRM vaccine.

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

Dosage and administration details:

One 0.5 mL injection of MenACWY was administered IM in the anterolateral area of the right thigh.

Arm title	MenACWY-TT (12 to 15 months old)

Arm description:

Subjects received one dose of comparator MenACWY-TT vaccine.

Arm type	Active comparator
Investigational medicinal product name	Meningococcal group A, C, W-135 and Y conjugate vaccine (ACWY-TT, Nimenrix)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

One 0.5 mL injection of MenACWY was administered IM in the anterolateral area of the right thigh.

Number of subjects in period 1	MenACWY-CRM (12 to 15 months old)	MenACWY-TT (12 to 15 months old)
Started	100	102
Completed	99	99
Not completed	1	3
Consent withdrawn by subject	1	-
Lost to follow-up	-	3

Baseline characteristics

Reporting groups	
Reporting group title	MenACWY-CRM (12 to 15 months old)
Reporting group description:	
Subjects received one dose of investigational MenACWY-CRM vaccine.	
Reporting group title	MenACWY-TT (12 to 15 months old)
Reporting group description:	
Subjects received one dose of comparator MenACWY-TT vaccine.	

Reporting group values	MenACWY-CRM (12 to 15 months old)	MenACWY-TT (12 to 15 months old)	Total
Number of subjects	100	102	202
Age categorical Units: Subjects			
Age continuous Units: months			
arithmetic mean	12.8	12.7	
standard deviation	± 1	± 0.9	-
Gender categorical Units: Subjects			
Female	48	46	94
Male	52	56	108

End points

End points reporting groups

Reporting group title	MenACWY-CRM (12 to 15 months old)
Reporting group description:	
Subjects received one dose of investigational MenACWY-CRM vaccine.	
Reporting group title	MenACWY-TT (12 to 15 months old)
Reporting group description:	
Subjects received one dose of comparator MenACWY-TT vaccine.	
Subject analysis set title	All enrolled set
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All subjects who provide informed consent and received a Subject Number.	
Subject analysis set title	All Exposed Set
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All subjects in the Enrolled Set who receive a study vaccination.	
Subject analysis set title	FAS Immunogenicity, Day 180
Subject analysis set type	Full analysis
Subject analysis set description:	
All subjects in the enrolled set who: received the study vaccine and provided immunogenicity data at visit Day 180.	
Subject analysis set title	Per Protocol Set (PPS), Immunogenicity, Day 29
Subject analysis set type	Per protocol
Subject analysis set description:	
All subjects in the FAS Immunogenicity who: - were not excluded due to reasons defined prior to unblinding or - analysis had no major protocol deviations. Exclusions were considered by objective/time point (Visit Day 29 and visit Day 180).	
Subject analysis set title	Full Analysis Set (FAS) Immunogenicity, Day 29
Subject analysis set type	Full analysis
Subject analysis set description:	
All subjects in the enrolled set who received the study vaccine and provided immunogenicity data at visit Day 29.	

Subject analysis set title	PPS, Immunogenicity, Day 180
Subject analysis set type	Per protocol
Subject analysis set description:	
All subjects in the FAS Immunogenicity who: - were not excluded due to reasons defined prior to unblinding or - analysis had no major protocol deviations. Exclusions were considered by objective/time point (Visit Day 29 and visit Day 180).	

Primary: 1. Number of subjects reporting at least one severe solicited adverse event (AE) after receiving one dose of either MenACWY-CRM vaccine or MenACWY-TT vaccine.

End point title	1. Number of subjects reporting at least one severe solicited adverse event (AE) after receiving one dose of either MenACWY-CRM vaccine or MenACWY-TT vaccine.[1]
End point description:	
Reactogenicity of MenACWY-CRM and comparator MenACWY-TT vaccine was assessed in subjects (12 to 15 months old) as measured by number of subjects with at least one severe solicited AE within 7 days after vaccination. Solicited AEs included tenderness, erythema, induration, irritability, sleepiness, change in eating habits, vomiting, diarrhea and fever. Analysis was done on solicited safety data set ie, all subjects in the exposed set who provided post-vaccination reactogenicity data.	

End point type	Primary

End point timeframe:

Day 1 to Day 7 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: statistical analyses not applicable.

End point values	MenACWY-CRM (12 to 15 months old)	MenACWY-TT (12 to 15 months old)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	99	101		
Units: Number of Subjects				
Severe solicited AEs	4	2		

Statistical analyses

No statistical analyses for this end point

Secondary: 2. Percentages of subjects with human Serum Bactericidal Assay (hSBA) titer ≥ 8 against N. meningitidis serogroups A, C, W, and Y after receiving one dose of either MenACWY-CRM vaccine or MenACWY-TT vaccine.

End point title	2. Percentages of subjects with human Serum Bactericidal Assay (hSBA) titer ≥ 8 against N. meningitidis serogroups A, C, W, and Y after receiving one dose of either MenACWY-CRM vaccine or MenACWY-TT vaccine.

End point description:

Immunogenicity of one dose of MenACWY-CRM and comparator MenACWY-TT vaccine was assessed in subjects (12 to 15 months old) as measured by the percentages of subjects with hSBA titer ≥ 8 directed against Neisseria meningitidis (N. meningitidis) serogroups A, C, W, and Y on Day 29 after vaccination. Persistence of immune responses was measured by the percentages of subjects with hSBA titer ≥ 8 on Day 180 post-vaccination. Analysis was done on FAS at Visit Day 29 ie, all subjects in the enrolled set who received the study vaccine and provided immunogenicity data at Visit Day 29 (MenACWY-CRM 95; MenACWT-TT 97). Persistence of immune responses at Day 180 was analysed on FAS at Visit Day 180, ie, all subjects in the enrolled set who received the study vaccine and provide immunogenicity data at Visit Day 180 (Men ACWY-CRM 98; MenACWT-TT 97).

End point type	Secondary

End point timeframe:

Day 1, Day 29 and Day 180 post-vaccination.

End point values	MenACWY-CRM (12 to 15 months old)	MenACWY-TT (12 to 15 months old)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	98	97		
Units: Percentages of Subjects				
number (confidence interval 95%)				
A Day 1 (N=89,92)	2 (0.27 to 7.9)	0 (0 to 3.9)		
A Day 29 (N=91,97)	90 (82.1 to 95.4)	88 (79.4 to 93.4)		

A Day 180 (N=97,96)	65 (54.6 to 74.4)	30 (21.3 to 40.4)		
C Day 1 (N=92,93)	3 (0.7 to 9.2)	1 (0.03 to 5.8)		
C Day 29 (N=94,97)	96 (89.5 to 98.8)	86 (77 to 91.9)		
C Day 180 (N=96,95)	88 (79.2 to 93.4)	95 (88.1 to 98.3)		
W Day 1 (N=81,78)	6 (2 to 13.8)	4 (0.8 to 10.8)		
W Day 29 (N=84,87)	62 (50.7 to 72.3)	72 (61.8 to 81.5)		
W Day 180 (N=88,89)	88 (78.7 to 93.6)	100 (95.9 to 100)		
Y Day 1 (84,84)	4 (0.7 to 10.1)	2 (0.29 to 8.3)		
Y Day 29 (N=87,91)	41 (30.9 to 52.4)	56 (45.2 to 66.4)		
Y Day 180 (N=92,95)	78 (68.4 to 86.2)	98 (92.6 to 99.74)		

Statistical analyses

No statistical analyses for this end point

Secondary: 3. Percentages of subjects with seroresponse against N. meningitidis against serogroups A, C, W, and Y after receiving one dose of either MenACWY-CRM vaccine or MenACWY-TT vaccine.

End point title	3. Percentages of subjects with seroresponse against N. meningitidis against serogroups A, C, W, and Y after receiving one dose of either MenACWY-CRM vaccine or MenACWY-TT vaccine.

End point description:

Immunogenicity of one dose of MenACWY-CRM and comparator MenACWY-TT vaccine was assessed in subjects (12 to 15 months old) as measured by the percentages of subjects with seroresponse defined as for subjects with pre-vaccination hSBA titer < 4, post-vaccination hSBA titer ≥ 8; for subjects with pre-vaccination hSBA titer ≥ 4, an increase of at least four times the pre-vaccination hSBA directed against N. meningitidis serogroups A, C, W, and Y on Day 29 after vaccination. Persistence immune response was measured by the percentages of subjects with seroresponse at Day 180 after vaccination. Analysis was done on FAS at Visit Day 29 ie, all subjects who received the study vaccine and provided immunogenicity data at Visit Day 29 (MenACWY-CRM 95; MenACWT-TT 97). Persistence of immune responses at Day 180 was analysed on FAS at Visit Day 180, ie, all subjects who received the study vaccine and provide immunogenicity data at Visit Day 180 (Men ACWY-CRM 98; MenACWT-TT 97).

End point type	Secondary

End point timeframe:

Day 29 and Day 180 post-vaccination.

End point values	MenACWY-CRM (12 to 15 months old)	MenACWY-TT (12 to 15 months old)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	98	97		
Units: Percentages of Subjects				
number (confidence interval 95%)				
A Day 29 (N=89,92)	88 (79 to 93.7)	87 (78.3 to 93.1)		

A Day 180 (N=95,92)	62 (51.6 to 71.9)	29 (20.3 to 39.8)		
C Day 29 (N=92,93)	95 (87.8 to 98.2)	84 (74.8 to 90.7)		
C Day 180 (N=94,92)	85 (76.3 to 91.6)	93 (86.3 to 97.6)		
W Day 29 (N=81,78)	54 (42.9 to 65.4)	73 (61.8 to 82.5)		
W Day 180 (N=83,81)	83 (73.3 to 90.5)	99 (93.3 to 99.97)		
Y Day 29 (N=84,84)	39 (28.8 to 50.5)	54 (42.4 to 64.5)		
Y Day 180 (N=88,87)	74 (63.4 to 82.7)	95 (88.6 to 98.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: 4. hSBA Geometric Mean Titers (GMTs) against N. meningitidis serogroups A, C, W, and Y after receiving one dose of either MenACWY-CRM vaccine or MenACWY-TT vaccine.

End point title	4. hSBA Geometric Mean Titers (GMTs) against N. meningitidis serogroups A, C, W, and Y after receiving one dose of either MenACWY-CRM vaccine or MenACWY-TT vaccine.

End point description:

Immunogenicity of one dose of MenACWY-CRM and comparator MenACWY-TT vaccine was assessed in subjects (12 to 15 months old) as measured by hSBA GMTs directed against N. meningitidis serogroups A, C, W, and Y on Day 29 after vaccination. Persistence of immune response was measured by hSBA GMTs at Day 180 after vaccination. Analysis was done on FAS at Visit Day 29 ie, all subjects in the enrolled set who received the study vaccine and provided immunogenicity data at Visit Day 29 (MenACWY-CRM 95; MenACWT-TT 97). Persistence of immune responses at Day 180 was analysed on FAS at Visit Day 180, ie, all subjects in the enrolled set who received the study vaccine and provide immunogenicity data at Visit Day 180 (Men ACWY-CRM 98; MenACWT-TT 97).

End point type	Secondary

End point timeframe:

Day 1, Day 29 and Day 180 post-vaccination.

End point values	MenACWY-CRM (12 to 15 months old)	MenACWY-TT (12 to 15 months old)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	98	97		
Units: Titers				
geometric mean (confidence interval 95%)				
A Day 1 (N=89,92)	2.19 (2.02 to 2.38)	2.04 (1.89 to 2.21)		
A Day 29 (N=91,97)	41 (31 to 55)	30 (23 to 40)		
A Day 180 (N=97,96)	13 (9.5 to 18)	4.67 (3.43 to 6.36)		
C Day 1 (N=92,93)	2.44 (2.16 to 2.76)	2.24 (1.99 to 2.52)		

C Day 29 (N=94,97)	30 (23 to 39)	20 (16 to 26)		
C Day 180 (N=96,95)	24 (18 to 30)	41 (32 to 53)		
W Day 1 (N=81,78)	2.58 (2.12 to 3.15)	2.4 (1.96 to 2.95)		
W day 29 (N=84,87)	9.34 (6.72 to 13)	14 (9.91 to 19)		
W Day 180 (N=88,89)	21 (17 to 27)	56 (45 to 70)		
Y Day 1 (N=84,84)	2.23 (2.02 to 2.48)	2.16 (1.94 to 2.4)		
Y Day 29 (N=87,91)	5.89 (4.27 to 8.13)	8.2 (5.96 to 11)		
Y Day 180 (N=92,95)	16 (12 to 21)	26 (20 to 34)		

Statistical analyses

No statistical analyses for this end point

Secondary: 5. Percentages of subjects with rabbit Serum Bactericidal Assay (rSBA) titer ≥ 8 against serogroups A, C, W, and Y after receiving one dose of either MenACWY-CRM vaccine or MenACWY-TT vaccine.

End point title	5. Percentages of subjects with rabbit Serum Bactericidal Assay (rSBA) titer ≥ 8 against serogroups A, C, W, and Y after receiving one dose of either MenACWY-CRM vaccine or MenACWY-TT vaccine.

End point description:

Immunogenicity of one dose of MenACWY-CRM and comparator MenACWY-TT vaccine was assessed in subjects (12 to 15 months old) as measured by the percentages of subjects with rSBA titer ≥ 8 directed against N. meningitidis serogroups A, C, W, and Y on Day 29 after vaccination. Persistence of immune response was measured by rSBA titer ≥ 8 on Day 180 after vaccination. Analysis was done on FAS at Visit Day 29 ie, all subjects in the enrolled set who received the study vaccine and provided immunogenicity data at Visit Day 29 (MenACWY-CRM 95; MenACWT-TT 97). Persistence of immune responses at Day 180 was analysed on FAS at Visit Day 180, ie, all subjects in the enrolled set who received the study vaccine and provide immunogenicity data at Visit Day 180 (Men ACWY-CRM 98; MenACWT-TT 97).

End point type	Secondary

End point timeframe:

Day 1, Day 29 and Day 180 post-vaccination.

End point values	MenACWY-CRM (12 to 15 months old)	MenACWY-TT (12 to 15 months old)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	98	97		
Units: Percentages of Subjects				
number (confidence interval 95%)				
A Day 1 (rabbit; N=63,61)	24 (14 to 36.2)	31 (19.9 to 44.3)		
A Day 29 (rabbit; N=73,74)	100 (95.1 to 100)	100 (95.1 to 100)		
A Day 180 (rabbit; N=74,75)	100 (95.1 to 100)	93 (85.1 to 97.8)		
C Day 1 (rabbit; N=64,62)	3 (0.38 to 10.8)	0 (0 to 5.8)		

C Day 29 (rabbit; N=74,74)	92 (83.2 to 97)	97 (90.6 to 99.67)		
C Day 180 (rabbit; N=77,76)	64 (51.9 to 74.3)	71 (59.5 to 80.9)		
W Day 1 (rabbit; N=61,57)	7 (1.8 to 15.9)	5 (1.1 to 14.6)		
W Day 29 (rabbit; N=70,69)	90 (80.5 to 95.9)	91 (82 to 96.7)		
W Day 180 (rabbit; N=73,70)	71 (59.4 to 81.2)	87 (77 to 93.9)		
Y Day 1 (rabbit; N=61,59)	10 (3.7 to 20.2)	15 (7.2 to 27)		
Y Day 29 (rabbit; N=70,70)	90 (80.5 to 95.9)	89 (78.7 to 94.9)		
Y Day 180 (rabbit; N=74,71)	80 (68.8 to 88.2)	82 (70.7 to 89.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: 6. Percentages of subjects with rSBA titer ≥ 128 against serogroups A, C, W, and Y after receiving one dose of either MenACWY-CRM vaccine or MenACWY-TT vaccine.

End point title	6. Percentages of subjects with rSBA titer ≥ 128 against serogroups A, C, W, and Y after receiving one dose of either MenACWY-CRM vaccine or MenACWY-TT vaccine.

End point description:

Immunogenicity of one dose of MenACWY-CRM and comparator MenACWY-TT vaccine was assessed in subjects (12 to 15 months old) as measured by the percentages of subjects with rSBA titer ≥ 128 directed against N. meningitidis serogroups A, C, W, and Y on Day 29 after vaccination. Persistence of immune responses was measured by percentages of subjects with rSBA titer ≥ 128 on Day 180. Analysis was done on FAS at Visit Day 29 ie, all subjects in the enrolled set who received the study vaccine and provided immunogenicity data at Visit Day 29 (MenACWY-CRM 95; MenACWT-TT 97). Persistence of immune responses at Day 180 was analysed on FAS at Visit Day 180, ie, all subjects in the enrolled set who received the study vaccine and provide immunogenicity data at Visit Day 180 (Men ACWY-CRM 98; MenACWT-TT 97).

End point type	Secondary

End point timeframe:

Day 1, Day 29 and Day 180 post-vaccination.

End point values	MenACWY-CRM (12 to 15 months old)	MenACWY-TT (12 to 15 months old)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	98	97		
Units: Percentages of Subjects				
number (confidence interval 95%)				
A Day 1 (rabbit; N=63,61)	22 (12.7 to 34.5)	31 (19.9 to 44.3)		
A Day 29 (rabbit; N=73,74)	100 (95.1 to 100)	100 (95.1 to 100)		
A Day 180 (rabbit; N=74,75)	100 (95.1 to 100)	91 (81.7 to 96.2)		

C Day 1 (rabbit; N=64,62)	3 (0.38 to 10.8)	0 (0 to 5.8)		
C Day 29 (rabbit; N=74,74)	78 (67.3 to 87.1)	65 (52.9 to 75.6)		
C Day 180 (rabbit; N=77,76)	25 (15.6 to 35.8)	33 (22.5 to 44.6)		
W Day 1 (rabbit; N=61,57)	7 (1.8 to 15.9)	5 (1.1 to 14.6)		
W Day 29 (rabbit; N=70,69)	90 (80.5 to 95.9)	90 (80.2 to 95.8)		
W Day 180 (rabbit; N=73,70)	62 (49.5 to 72.8)	66 (53.4 to 76.7)		
Y Day 1 (rabbit; N=61,59)	10 (3.7 to 20.2)	12 (4.9 to 22.9)		
Y Day 29 (rabbit; N=70,70)	89 (78.7 to 94.9)	86 (75.3 to 92.9)		
Y Day 180 (rabbit; N=74,71)	73 (61.4 to 82.6)	62 (49.7 to 73.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: 7. Percentages of subjects with four-fold increase in rSBA titers against serogroups A, C, W, and Y after receiving one dose of either MenACWY-CRM vaccine or MenACWY-TT vaccine.

End point title	7. Percentages of subjects with four-fold increase in rSBA titers against serogroups A, C, W, and Y after receiving one dose of either MenACWY-CRM vaccine or MenACWY-TT vaccine.

End point description:

Immunogenicity of one dose of MenACWY-CRM and comparator MenACWY-TT vaccine was assessed in subjects (12 to 15 months old) as measured by the percentages of subjects with four-fold increase in rSBA titer directed against N. meningitides serogroups A, C, W, and Y on Day 29 after vaccination. Persistence of immune responses was measured by the percentages of subjects with four-fold increase in rSBA titer on Day 180 after vaccination. Analysis was done on FAS at Visit Day 29 ie, all subjects in the enrolled set who received the study vaccine and provided immunogenicity data at Visit Day 29 (MenACWY-CRM 95; MenACWT-TT 97). Persistence of immune responses at Day 180 was analysed on FAS at Visit Day 180, ie, all subjects in the enrolled set who received the study vaccine and provide immunogenicity data at Visit Day 180 (Men ACWY-CRM 98; MenACWT-TT 97).

End point type	Secondary

End point timeframe:

Day 29 and Day 180 post-vaccination.

End point values	MenACWY-CRM (12 to 15 months old)	MenACWY-TT (12 to 15 months old)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	98	97		
Units: Percentages of Subjects				
number (confidence interval 95%)				
A Day 29 (rabbit; N=63,61)	100 (94.3 to 100)	93 (84.1 to 98.2)		
A Day 180 (rabbit; N=60,61)	97 (88.5 to 99.59)	84 (71.9 to 91.8)		

C Day 29 (rabbit; N=64,62)	75 (62.6 to 85)	65 (51.3 to 76.3)		
C Day 180 (rabbit; N=64,63)	20 (11.3 to 32.2)	30 (19.2 to 43)		
W Day 29 (rabbit; N=61,57)	87 (75.8 to 94.2)	89 (78.5 to 96)		
W Day 180 (rabbit; N=58,58)	55 (41.5 to 68.3)	66 (51.9 to 77.5)		
Y Day 29 (rabbit; N=61,59)	87 (75.8 to 94.2)	88 (77.1 to 95.1)		
Y Day 180 (rabbit; N=61,59)	72 (59.2 to 82.9)	56 (42.4 to 68.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: 8. rSBA GMT against N. meningitidis against serogroups A, C, W, and Y after receiving one dose of either MenACWY-CRM vaccine or MenACWY-TT vaccine.

End point title	8. rSBA GMT against N. meningitidis against serogroups A, C, W, and Y after receiving one dose of either MenACWY-CRM vaccine or MenACWY-TT vaccine.

End point description:

Immunogenicity of one dose of MenACWY-CRM and comparator MenACWY-TT vaccine was assessed in subjects (12 to 15 months old) as measured by rSBA GMTs directed against N. meningitidis serogroups A, C, W, and Y on Day 29 after vaccination. Persistence of immune responses was measured by rSBA GMTs on Day 180.Analysis was done on FAS at Visit Day 29 ie, all subjects in the enrolled set who received the study vaccine and provided immunogenicity data at Visit Day 29 (MenACWY-CRM 95; MenACWT-TT 97). Persistence of immune responses at Day 180 was analysed on FAS at Visit Day 180, ie, all subjects in the enrolled set who received the study vaccine and provide immunogenicity data at Visit Day 180 (Men ACWY-CRM 98; MenACWT-TT 97).

End point type	Secondary

End point timeframe:

Day 1, Day 29 and Day 180 post-vaccination.

End point values	MenACWY-CRM (12 to 15 months old)	MenACWY-TT (12 to 15 months old)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	98	97		
Units: Titers				
geometric mean (confidence interval 95%)				
A Day 1 (rabbit; N=63,61)	6.62 (3.12 to 14)	12 (5.59 to 26)		
A Day 29 (rabbit; N=73,74)	5698 (4226 to 7684)	2827 (2116 to 3775)		
A Day 180 (rabbit; N=74,75)	2815 (1741 to 4550)	950 (592 to 1523)		
C Day 1 (rabbit; N=64,62)	2.46 (1.98 to 3.05)	2.07 (1.66 to 2.58)		
C Day 29 (rabbit; N=74,74)	171 (113 to 259)	142 (95 to 213)		
C Day 180 (rabbit; N=77,76)	20 (12 to 33)	22 (13 to 36)		

W Day 1 (rabbit; N=61,57)	3.1 (2.09 to 4.59)	3.17 (2.07 to 4.86)		
W Day 29 (rabbit; N=70,69)	1092 (570 to 2089)	1060 (553 to 2031)		
W Day 180 (rabbit; N=73,70)	91 (46 to 182)	142 (72 to 282)		
Y Day 1 (rabbit; N=61,59)	3.46 (2.03 to 5.89)	4.22 (2.42 to 7.38)		
Y Day 29 (rabbit; N=70,70)	756 (400 to 1429)	624 (333 to 1168)		
Y Day 180 (rabbit; N=74,71)	248 (124 to 495)	140 (70 to 278)		

Statistical analyses

No statistical analyses for this end point

Secondary: 9. Number of subjects reporting solicited adverse events (AEs) after receiving one dose of either MenACWY-CRM vaccine or MenACWY-TT vaccine.

End point title	9. Number of subjects reporting solicited adverse events (AEs) after receiving one dose of either MenACWY-CRM vaccine or MenACWY-TT vaccine.

End point description:

Safety was assessed in terms of number of subjects (12 to 15 months old) reporting any and each of solicited local and systemic AEs, reported from Day 1 to 7 after vaccination, with one dose of either MenACWY-CRM or comparator MenACWY-TT vaccine. Analysis was done on solicited safety data set.

End point type	Secondary

End point timeframe:

Day 1 (6 hours) to Day 7 post-vaccination.

End point values	MenACWY-CRM (12 to 15 months old)	MenACWY-TT (12 to 15 months old)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	99	101		
Units: Subjects				
Any Local	34	29		
Tenderness (N=97,100)	29	26		
Erythema (N=97,100)	4	2		
Induration (N=97,101)	6	4		
Any Systemic	56	57		
Irritability (N=96,99)	30	39		
Sleepiness (N=96,98)	23	26		
Change in eating habits (N=96,100)	22	26		
Vomiting (N=96,99)	6	9		
Diarrhea (N=96,99)	17	18		
Fever (≥ 38.0°C; N=99,100)	14	13		
Prophylatic use of analg./antipyr. (N=97,100)	1	4		
Therapeutic use of analg./antipyr. (N=98,100)	13	13		

Statistical analyses

No statistical analyses for this end point

Secondary: 10. Number of subjects reporting unsolicited adverse events (AEs) after receiving one dose of either MenACWY-CRM vaccine or MenACWY-TT vaccine.

End point title	10. Number of subjects reporting unsolicited adverse events (AEs) after receiving one dose of either MenACWY-CRM vaccine or MenACWY-TT vaccine.

End point description:

Safety was assessed in terms of number of subjects (12 to 15 months old) reporting unsolicited AEs (Day 1 to Day 29), Serious Adverse Events (SAEs), medically attended AEs, AEs leading to premature study withdrawal (Day 1 to Day 180) after vaccination with one dose of either MenACWY-CRM or comparator MenACWY-TT vaccine. Analysis was done on unsolicited safety data set ie, all subjects in the exposed set who had post-vaccination unsolicited adverse event records.

End point type	Secondary

End point timeframe:

Day 1 to Day 29 or Day 1 to Day 180 post-vaccination.

End point values	MenACWY-CRM (12 to 15 months old)	MenACWY-TT (12 to 15 months old)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	99	101		
Units: Subjects				
Any unsolicited AEs	73	71		
AEs leading to premature withdrawal	0	0		
SAEs	8	3		
Medically attended AEs	73	68		
Death	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited AEs were collected from Day 1 to Day 7 post vaccination, unsolicited AEs were collected from Day 1 to Day 29 post vaccination and SAEs, medically attended AEs and AEs leading to premature withdrawal were collected from Day 1 to Day 180.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	MenACWY-TT (12 to 15 months old)

Reporting group description:

Subjects received one dose of comparator MenACWY-TT vaccine.

Reporting group title	MenACWY-CRM (12 to 15 months old)

Reporting group description:

Subjects received one dose of investigational MenACWY-CRM vaccine.

Serious adverse events	MenACWY-TT (12 to 15 months old)	MenACWY-CRM (12 to 15 months old)	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 101 (2.97%)	8 / 99 (8.08%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Head injury			
subjects affected / exposed	0 / 101 (0.00%)	1 / 99 (1.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tongue injury			
subjects affected / exposed	0 / 101 (0.00%)	1 / 99 (1.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Febrile convulsion			
subjects affected / exposed	1 / 101 (0.99%)	1 / 99 (1.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal			

disorders			
Bronchospasm			
subjects affected / exposed	1 / 101 (0.99%)	0 / 99 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	0 / 101 (0.00%)	1 / 99 (1.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bacteraemia			
subjects affected / exposed	0 / 101 (0.00%)	1 / 99 (1.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	0 / 101 (0.00%)	1 / 99 (1.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis rotavirus			
subjects affected / exposed	1 / 101 (0.99%)	0 / 99 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rotavirus infection			
subjects affected / exposed	0 / 101 (0.00%)	2 / 99 (2.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	MenACWY-TT (12 to 15 months old)	MenACWY-CRM (12 to 15 months old)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	87 / 101 (86.14%)	83 / 99 (83.84%)	
Nervous system disorders			

Somnolence			
subjects affected / exposed	27 / 101 (26.73%)	23 / 99 (23.23%)	
occurrences (all)	30	26	
General disorders and administration site conditions			
Injection site induration			
subjects affected / exposed	26 / 101 (25.74%)	25 / 99 (25.25%)	
occurrences (all)	26	26	
Injection site pain			
subjects affected / exposed	27 / 101 (26.73%)	29 / 99 (29.29%)	
occurrences (all)	27	30	
Pyrexia			
subjects affected / exposed	34 / 101 (33.66%)	31 / 99 (31.31%)	
occurrences (all)	48	44	
Injection site erythema			
subjects affected / exposed	27 / 101 (26.73%)	26 / 99 (26.26%)	
occurrences (all)	27	26	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	22 / 101 (21.78%)	21 / 99 (21.21%)	
occurrences (all)	29	26	
Vomiting			
subjects affected / exposed	11 / 101 (10.89%)	8 / 99 (8.08%)	
occurrences (all)	13	10	
Respiratory, thoracic and mediastinal disorders			
Bronchospasm			
subjects affected / exposed	8 / 101 (7.92%)	1 / 99 (1.01%)	
occurrences (all)	12	1	
Cough			
subjects affected / exposed	8 / 101 (7.92%)	9 / 99 (9.09%)	
occurrences (all)	8	11	
Upper respiratory tract inflammation			
subjects affected / exposed	4 / 101 (3.96%)	9 / 99 (9.09%)	
occurrences (all)	4	10	
Skin and subcutaneous tissue disorders			
Rash			

subjects affected / exposed	1 / 101 (0.99%)	5 / 99 (5.05%)	
occurrences (all)	1	5	
Psychiatric disorders			
Eating disorder			
subjects affected / exposed	26 / 101 (25.74%)	22 / 99 (22.22%)	
occurrences (all)	28	27	
Irritability			
subjects affected / exposed	40 / 101 (39.60%)	30 / 99 (30.30%)	
occurrences (all)	46	37	
Infections and infestations			
Ear infection			
subjects affected / exposed	4 / 101 (3.96%)	15 / 99 (15.15%)	
occurrences (all)	4	20	
Conjunctivitis			
subjects affected / exposed	8 / 101 (7.92%)	6 / 99 (6.06%)	
occurrences (all)	9	7	
Rhinitis			
subjects affected / exposed	2 / 101 (1.98%)	5 / 99 (5.05%)	
occurrences (all)	2	5	
Exanthema subitum			
subjects affected / exposed	5 / 101 (4.95%)	7 / 99 (7.07%)	
occurrences (all)	5	7	
Gastroenteritis			
subjects affected / exposed	6 / 101 (5.94%)	2 / 99 (2.02%)	
occurrences (all)	6	2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 February 2014	The end of study was defined in compliance with a newly implemented Novartis policy. Duration of collection of concomitant medications was changed to 28 days after vaccination only, instead of collection over the entire study duration. Minor inconsistencies and typographical errors have been corrected.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported