



Clinical trial results:

A Phase 2b, Open-Label, Multi-Center Study to Evaluate the Persistence of Antibody Response and to Assess the Immune Response to a Booster Dose of MenACWY Conjugate Vaccine in Subjects Previously Vaccinated as Adolescents with Either MenACWY Conjugate Vaccine or Menomune®

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

Summary

EudraCT number	2014-005059-25
Trial protocol	Outside EU/EEA
Global end of trial date	25 July 2010

Results information

Result version number	v2 (current)
This version publication date	04 June 2016
First version publication date	18 March 2015
Version creation reason	<ul style="list-style-type: none">• Correction of full data set re-QC needed to study because of EudraCT system glitch and updates to results are required.

Trial information

Trial identification

Sponsor protocol code	V59P6E1
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01018732
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Vaccines and Diagnostics Inc.
Sponsor organisation address	350 Massachusetts Ave, Cambridge, United States, 02139
Public contact	Posting Director, Novartis Vaccines and Diagnostics Inc., RegistryContactVaccinesUS@novartis.com
Scientific contact	Posting Director, Novartis Vaccines and 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 June 2011
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	25 July 2010
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

1. To evaluate the persistence of the antibody response at 5 years after one dose of MenACWY or Menomune®, as measured by the percentage of subjects with bactericidal activity using human complement (hSBA) $\geq 1:8$ directed against N. meningitidis serogroups A, C, W-135, and Y.
2. To evaluate the antibody response to one dose of MenACWY in subjects who had previously received one dose of MenACWY compared to the antibody response to one dose of MenACWY in meningococcal vaccine-naïve subjects, as measured by hSBA geometric mean titers (GMTs) directed against N. meningitidis serogroups A, C, W-135 and Y, at 28 days after vaccination.

Protection of trial subjects:

This clinical study was designed, implemented 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 with the ethical principles laid down in the Declaration of Helsinki.

Background therapy:

N/A

Evidence for comparator:

N/A

Actual start date of recruitment	19 January 2010
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 155
Worldwide total number of subjects	155
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)	0
Adolescents (12-17 years)	38
Adults (18-64 years)	117
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were enrolled at 3 centers in the US.

Pre-assignment

Screening details:

All subjects enrolled were included in the trial.

Period 1

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

Blinding implementation details:

The trial was designed as an open-label study; all subjects received the same vaccine, their allocation had been previously revealed to the sites after unblinding of the parent study. Subjects, investigators, and other study personnel were not blinded. The only personnel who were blinded were the data analysts and the laboratory personnel who received the sera.

Arms

Are arms mutually exclusive?	Yes
Arm title	MenACWY-CRM Vaccine

Arm description:

Subjects had been given one dose of Meningococcal (groups A, C, W, and Y) vaccine conjugated to CRM197 (cross-reactive material-mutant of diphtheria toxin) (MenACWY) 5 years ago.

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

Dosage and administration details:

One dose of 0.5mL.

Arm title	Licensed Polysaccharide Meningococcal Vaccine
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Arm description:

Subjects had been given one dose of licensed Men ACWY (Menomune®) 5 years ago.

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

Dosage and administration details:

One dose of 0.5mL.

Arm title	Meningococcal Naïve
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Arm description:

Subjects were between 16 years to 23 years (age-inclusive) and meningococcal vaccine naïve.

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

Dosage and administration details:

One dose of 0.5mL.

Number of subjects in period 1	MenACWY-CRM Vaccine	Licensed Polysaccharide Meningococcal Vaccine	Meningococcal Naïve
Started	50	51	54
Completed	49	49	50
Not completed	1	2	4
Unable to classify	-	-	1
Inappropriate enrolment	-	1	-
Lost to follow-up	-	-	3
Protocol deviation	1	1	-

Baseline characteristics

Reporting groups

Reporting group title	MenACWY-CRM Vaccine
Reporting group description:	
Subjects had been given one dose of Meningococcal (groups A, C, W, and Y) vaccine conjugated to CRM197 (cross-reactive material-mutant of diphtheria toxin) (MenACWY) 5 years ago.	
Reporting group title	Licensed Polysaccharide Meningococcal Vaccine
Reporting group description:	
Subjects had been given one dose of licensed Men ACWY (Menomune®) 5 years ago.	
Reporting group title	Meningococcal Naïve
Reporting group description:	
Subjects were between 16 years to 23 years (age-inclusive) and meningococcal vaccine naïve.	

Reporting group values	MenACWY-CRM Vaccine	Licensed Polysaccharide Meningococcal Vaccine	Meningococcal Naïve
Number of subjects	50	51	54
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years			
arithmetic mean	18.8	19.2	20.5
standard deviation	± 1.9	± 2	± 2.3
Gender categorical Units: Subjects			
Female	22	28	33
Male	28	23	21

Reporting group values	Total		
Number of subjects	155		
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years)	0 0 0 0 0		

Adolescents (12-17 years)	0		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Age continuous Units: years arithmetic mean standard deviation	-		
Gender categorical Units: Subjects			
Female	83		
Male	72		

Subject analysis sets

Subject analysis set title	Exposed Population
Subject analysis set type	Intention-to-treat
Subject analysis set description: All enrolled subjects who actually received the study vaccination.	
Subject analysis set title	Enrolled Population
Subject analysis set type	Intention-to-treat
Subject analysis set description: All subjects who signed an informed consent and underwent screening procedure(s).	
Subject analysis set title	FAS, Immunogenicity after one dose of MenACWY (FAS Booster)
Subject analysis set type	Full analysis
Subject analysis set description: All subjects who received the study vaccination, and provided at least one evaluable serum sample before or after baseline and whose assay result is available for at least one serogroup.	
Subject analysis set title	Full Analysis Set, Antibody Persistence (FAS Persist)
Subject analysis set type	Full analysis
Subject analysis set description: All subjects in the enrolled population with an evaluable blood sample at day 1 and whose assay result was available for at least one serogroup.	
Subject analysis set title	Safety Population
Subject analysis set type	Safety analysis
Subject analysis set description: All subjects in the Exposed Population who provided post-baseline safety data.	

Reporting group values	Exposed Population	Enrolled Population	FAS, Immunogenicity after one dose of MenACWY (FAS Booster)
Number of subjects	153	155	148
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years)			

Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous			
Units: years			
arithmetic mean		19.5	
standard deviation	±	± 2.1	±
Gender categorical			
Units: Subjects			
Female		83	
Male		72	

Reporting group values	Full Analysis Set, Antibody Persistence (FAS Persist)	Safety Population	
Number of subjects	153	153	
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous			
Units: years			
arithmetic mean			
standard deviation	±	±	
Gender categorical			
Units: Subjects			
Female			
Male			

End points

End points reporting groups

Reporting group title	MenACWY-CRM Vaccine
Reporting group description: Subjects had been given one dose of Meningococcal (groups A, C, W, and Y) vaccine conjugated to CRM197 (cross-reactive material-mutant of diphtheria toxin) (MenACWY) 5 years ago.	
Reporting group title	Licensed Polysaccharide Meningococcal Vaccine
Reporting group description: Subjects had been given one dose of licensed Men ACWY (Menomune®) 5 years ago.	
Reporting group title	Meningococcal Naïve
Reporting group description: Subjects were between 16 years to 23 years (age-inclusive) and meningococcal vaccine naïve.	
Subject analysis set title	Exposed Population
Subject analysis set type	Intention-to-treat
Subject analysis set description: All enrolled subjects who actually received the study vaccination.	
Subject analysis set title	Enrolled Population
Subject analysis set type	Intention-to-treat
Subject analysis set description: All subjects who signed an informed consent and underwent screening procedure(s).	
Subject analysis set title	FAS, Immunogenicity after one dose of MenACWY (FAS Booster)
Subject analysis set type	Full analysis
Subject analysis set description: All subjects who received the study vaccination, and provided at least one evaluable serum sample before or after baseline and whose assay result is available for at least one serogroup.	
Subject analysis set title	Full Analysis Set, Antibody Persistence (FAS Persist)
Subject analysis set type	Full analysis
Subject analysis set description: All subjects in the enrolled population with an evaluable blood sample at day 1 and whose assay result was available for at least one serogroup.	
Subject analysis set title	Safety Population
Subject analysis set type	Safety analysis
Subject analysis set description: All subjects in the Exposed Population who provided post-baseline safety data.	

Primary: 1. Percentages of Subjects With Serum Bactericidal Activity ≥ 8 at 5 Years After Primary Vaccination

End point title	1. Percentages of Subjects With Serum Bactericidal Activity ≥ 8 at 5 Years After Primary Vaccination ^[1]
End point description: Persistence of antibody response was measured by the percentages of subjects who showed hSBA ≥ 8 [i.e. percentages of subjects with hSBA titer ≥ 8] in previously vaccinated subjects and in age-matched meningococcal vaccine naïve subjects. Sera were tested against Neisseria meningitidis (N. Meningitidis) serogroups A, C, W-135 and Y. The analysis was done on the FAS, Antibody Persistence Population.	
End point type	Primary
End point timeframe: Day 1 (5 years after 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 analysis is associated to this endpoint. Analyses were run descriptively.

End point values	MenACWY-CRM Vaccine	Licensed Polysaccharide Meningococcal Vaccine	Meningococcal Naïve	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	50	50	53	
Units: Percentages of Subjects				
number (confidence interval 95%)				
Men A	30 (18 to 45)	44 (30 to 59)	11 (4 to 23)	
Men C	76 (62 to 87)	62 (47 to 75)	51 (37 to 65)	
Men W-135	72 (58 to 84)	56 (41 to 70)	51 (37 to 65)	
Men Y	76 (62 to 87)	50 (36 to 64)	55 (40 to 68)	

Statistical analyses

No statistical analyses for this end point

Primary: 2. Geometric Mean Titer After Booster Vaccination

End point title	2. Geometric Mean Titer After Booster Vaccination
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End point description:

Immunogenicity was measured by hSBA and reported as hSBA Geometric Mean Titer (GMT) in previously vaccinated subjects and in age-matched meningococcal vaccine-naïve subjects. Sera was tested against *Neisseria meningitidis* serogroups A, C, W-135 and Y.

The analysis was done on the FAS, Immunogenicity after one dose of MenACWY (FAS Booster) Population.

End point type	Primary
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End point timeframe:

Day 8, Day 29 (after a booster at 5 years after primary vaccination).

End point values	MenACWY-CRM Vaccine	Licensed Polysaccharide Meningococcal Vaccine	Meningococcal Naïve	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	49	49	50	
Units: Titers				
geometric mean (confidence interval 95%)				
Baseline, Men A	5.16 (3.46 to 7.7)	7.31 (4.94 to 11)	3.06 (2.06 to 4.55)	
Day 8, Men A	1059 (585 to 1917)	45 (25 to 80)	34 (19 to 61)	
Day 29, Men A, (N=48, 49, 50)	819 (514 to 1305)	147 (94 to 232)	113 (72 to 179)	
Baseline, Men C	20 (13 to 33)	19 (12 to 31)	7.34 (4.6 to 12)	

Day 8, Men C	1603 (893 to 2877)	36 (20 to 64)	70 (39 to 124)	
Day 29, Men C	1217 (717 to 2066)	51 (30 to 86)	127 (75 to 214)	
Baseline, Men W-135	29 (17 to 49)	12 (7.02 to 19)	11 (6.31 to 18)	
Day 8, Men W-135	1685 (1042 to 2725)	34 (21 to 54)	63 (39 to 101)	
Day 29, Men W-135	1644 (1090 to 2481)	47 (32 to 71)	79 (52 to 118)	
Baseline, Men Y	28 (18 to 45)	7.8 (4.91 to 12)	8.69 (5.45 to 14)	
Day 8, Men Y, (N=48, 49, 50)	2561 (1526 to 4298)	21 (13 to 35)	64 (39 to 107)	
Day 29, Men Y	2092 (1340 to 3268)	63 (41 to 98)	110 (70 to 170)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1 for GMT After Booster
Statistical analysis description: Day 1 (Pre-booster), Men A, Pairwise comparison of geometric mean titer.	
Comparison groups	Meningococcal Naïve v Licensed Polysaccharide Meningococcal Vaccine
Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	Vaccine Group Ratios
Point estimate	2.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.39
upper limit	4.1

Statistical analysis title	Statistical Analysis 2 for GMT After Booster
Statistical analysis description: Day 1 (Pre-booster), Men A, Pairwise comparison of geometric mean titer.	
Comparison groups	Licensed Polysaccharide Meningococcal Vaccine v MenACWY-CRM Vaccine
Number of subjects included in analysis	98
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	Vaccine Group Ratios
Point estimate	0.71

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.42
upper limit	1.2

Statistical analysis title	Statistical Analysis 3 for GMT After Booster
Statistical analysis description:	
Day 1 (Pre-booster), Men A, Pairwise comparison of geometric mean titer.	
Comparison groups	Meningococcal Naïve v MenACWY-CRM Vaccine
Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	Vaccine Group Ratios
Point estimate	1.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.98
upper limit	2.9

Statistical analysis title	Statistical Analysis 4 for GMT After Booster
Statistical analysis description:	
Day 8, Men A, Pairwise comparison of geometric mean titer.	
Comparison groups	Meningococcal Naïve v Licensed Polysaccharide Meningococcal Vaccine
Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	Vaccine Group Ratios
Point estimate	1.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.59
upper limit	2.91

Statistical analysis title	Statistical Analysis 5 for GMT After Booster
Statistical analysis description:	
Day 8, Men A, Pairwise comparison of geometric mean titer.	
Comparison groups	Licensed Polysaccharide Meningococcal Vaccine v MenACWY-CRM Vaccine

Number of subjects included in analysis	98
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	Vaccine Group Ratios
Point estimate	24
Confidence interval	
level	95 %
sides	2-sided
lower limit	11
upper limit	52

Statistical analysis title	Statistical Analysis 6 for GMT After Booster
Statistical analysis description: Day 8, Men A, Pairwise comparison of geometric mean titer.	
Comparison groups	MenACWY-CRM Vaccine v Meningococcal Naïve
Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	Vaccine Group Ratios
Point estimate	31
Confidence interval	
level	95 %
sides	2-sided
lower limit	14
upper limit	69

Statistical analysis title	Statistical Analysis 7 for GMT After Booster
Statistical analysis description: Day 29, Men A, Pairwise comparison of geometric mean titer.	
Comparison groups	Meningococcal Naïve v Licensed Polysaccharide Meningococcal Vaccine
Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	Vaccine Group Ratios
Point estimate	1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	2.42

Statistical analysis title	Statistical Analysis 8 for GMT After Booster
Statistical analysis description: Day 29, Men A, Pairwise comparison of geometric mean titer.	
Comparison groups	Licensed Polysaccharide Meningococcal Vaccine v MenACWY-CRM Vaccine
Number of subjects included in analysis	98
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	Vaccine Group Ratios
Point estimate	5.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.01
upper limit	10

Statistical analysis title	Statistical Analysis 9 for GMT After Booster
Statistical analysis description: Day 29, Men A, Pairwise comparison of geometric mean titer.	
Comparison groups	MenACWY-CRM Vaccine v Meningococcal Naïve
Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	Vaccine Group Ratios
Point estimate	7.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.86
upper limit	13

Statistical analysis title	Statistical Analysis 10 for GMT After Booster
Statistical analysis description: Day 1 (Pre-booster), Men C, Pairwise comparison of geometric mean titer.	
Comparison groups	Meningococcal Naïve v Licensed Polysaccharide Meningococcal Vaccine

Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	Vaccine Group Ratios
Point estimate	2.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.4
upper limit	4.99

Statistical analysis title	Statistical Analysis 11 for GMT After Booster
Statistical analysis description: Day 1 (Pre-booster), Men C, Pairwise comparison of geometric mean titer.	
Comparison groups	Licensed Polysaccharide Meningococcal Vaccine v MenACWY-CRM Vaccine
Number of subjects included in analysis	98
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	Vaccine Group Ratios
Point estimate	1.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.56
upper limit	1.97

Statistical analysis title	Statistical Analysis 12 for GMT After Booster
Statistical analysis description: Day 1 (Pre-booster), Men C, Pairwise comparison of geometric mean titer.	
Comparison groups	MenACWY-CRM Vaccine v Meningococcal Naïve
Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	Vaccine Group Ratios
Point estimate	2.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.47
upper limit	5.27

Statistical analysis title	Statistical Analysis 13 for GMT After Booster
Statistical analysis description: Day 8, Men C, Pairwise comparison of geometric mean titer.	
Comparison groups	Meningococcal Naïve v Licensed Polysaccharide Meningococcal Vaccine
Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	Vaccine Group Ratios
Point estimate	0.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.23
upper limit	1.13

Statistical analysis title	Statistical Analysis 14 for GMT After Booster
Statistical analysis description: Day 8, Men C, Pairwise comparison of geometric mean titer.	
Comparison groups	MenACWY-CRM Vaccine v Licensed Polysaccharide Meningococcal Vaccine
Number of subjects included in analysis	98
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	Vaccine Group Ratios
Point estimate	45
Confidence interval	
level	95 %
sides	2-sided
lower limit	21
upper limit	97

Statistical analysis title	Statistical Analysis 15 for GMT After Booster
Statistical analysis description: Day 8, Men C, Pairwise comparison of geometric mean titer.	
Comparison groups	Meningococcal Naïve v MenACWY-CRM Vaccine

Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	Vaccine Group Ratios
Point estimate	23
Confidence interval	
level	95 %
sides	2-sided
lower limit	10
upper limit	51

Statistical analysis title	Statistical Analysis 16 for GMT After Booster
Statistical analysis description: Day 29, Men C, Pairwise comparison of geometric mean titer.	
Comparison groups	Meningococcal Naïve v Licensed Polysaccharide Meningococcal Vaccine
Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	Vaccine Group Ratios
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.2
upper limit	0.82

Statistical analysis title	Statistical Analysis 17 for GMT After Booster
Statistical analysis description: Day 29, Men C, Pairwise comparison of geometric mean titer.	
Comparison groups	Licensed Polysaccharide Meningococcal Vaccine v MenACWY-CRM Vaccine
Number of subjects included in analysis	98
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	Vaccine Group Ratios
Point estimate	24
Confidence interval	
level	95 %
sides	2-sided
lower limit	12
upper limit	48

Statistical analysis title	Statistical Analysis 18 for GMT After Booster
Statistical analysis description: Day 29, Men C, Pairwise comparison of geometric mean titer.	
Comparison groups	MenACWY-CRM Vaccine v Meningococcal Naïve
Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	Vaccine Group Ratios
Point estimate	9.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.69
upper limit	20

Statistical analysis title	Statistical Analysis 19 for GMT After Booster
Statistical analysis description: Day 1 (Pre-booster), Men W-135, Pairwise comparison of geometric mean titer.	
Comparison groups	Meningococcal Naïve v Licensed Polysaccharide Meningococcal Vaccine
Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	Vaccine Group Ratios
Point estimate	1.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.55
upper limit	2.21

Statistical analysis title	Statistical Analysis 20 for GMT After Booster
Statistical analysis description: Day 1 (Pre-booster), Men W-135, Pairwise comparison of geometric mean titer.	
Comparison groups	Licensed Polysaccharide Meningococcal Vaccine v MenACWY-CRM Vaccine

Number of subjects included in analysis	98
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	Vaccine Group Ratios
Point estimate	2.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.27
upper limit	4.96

Statistical analysis title	Statistical Analysis 21 for GMT After Booster
Statistical analysis description:	
Day 1 (Pre-booster), Men W-135, Pairwise comparison of geometric mean titer.	
Comparison groups	MenACWY-CRM Vaccine v Meningococcal Naïve
Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	Vaccine Group Ratios
Point estimate	2.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.38
upper limit	5.57

Statistical analysis title	Statistical Analysis 22 for GMT After Booster
Statistical analysis description:	
Day 8, Men W-135, Pairwise comparison of geometric mean titer.	
Comparison groups	Meningococcal Naïve v Licensed Polysaccharide Meningococcal Vaccine
Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	Vaccine Group Ratios
Point estimate	0.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.28
upper limit	1.04

Statistical analysis title	Statistical Analysis 23 for GMT After Booster
Statistical analysis description: Day 8, Men W-135, Pairwise comparison of geometric mean titer.	
Comparison groups	Licensed Polysaccharide Meningococcal Vaccine v MenACWY-CRM Vaccine
Number of subjects included in analysis	98
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	Vaccine Group Ratios
Point estimate	50
Confidence interval	
level	95 %
sides	2-sided
lower limit	26
upper limit	94

Statistical analysis title	Statistical Analysis 24 for GMT After Booster
Statistical analysis description: Day 8, Men W-135, Pairwise comparison of geometric mean titer.	
Comparison groups	MenACWY-CRM Vaccine v Meningococcal Naïve
Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	Vaccine Group Ratios
Point estimate	27
Confidence interval	
level	95 %
sides	2-sided
lower limit	14
upper limit	52

Statistical analysis title	Statistical Analysis 25 for GMT After Booster
Statistical analysis description: Day 29, Men W-135, Pairwise comparison of geometric mean titer.	
Comparison groups	Meningococcal Naïve v Licensed Polysaccharide Meningococcal Vaccine

Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	Vaccine Group Ratios
Point estimate	0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.34
upper limit	1.04

Statistical analysis title	Statistical Analysis 26 for GMT After Booster
Statistical analysis description: Day 29, Men W-135, Pairwise comparison of geometric mean titer.	
Comparison groups	Licensed Polysaccharide Meningococcal Vaccine v MenACWY-CRM Vaccine
Number of subjects included in analysis	98
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	Vaccine Group Ratios
Point estimate	35
Confidence interval	
level	95 %
sides	2-sided
lower limit	20
upper limit	60

Statistical analysis title	Statistical Analysis 27 for GMT After Booster
Statistical analysis description: Day 29, Men W-135, Pairwise comparison of geometric mean titer.	
Comparison groups	MenACWY-CRM Vaccine v Meningococcal Naïve
Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	Vaccine Group Ratios
Point estimate	21
Confidence interval	
level	95 %
sides	2-sided
lower limit	12
upper limit	36

Statistical analysis title	Statistical Analysis 28 for GMT After Booster
Statistical analysis description: Day 1 (Pre-booster), Men Y, Pairwise comparison of geometric mean titer.	
Comparison groups	Meningococcal Naïve v Licensed Polysaccharide Meningococcal Vaccine
Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	Vaccine Group Ratios
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.48
upper limit	1.69

Statistical analysis title	Statistical Analysis 29 for GMT After Booster
Statistical analysis description: Day 1 (Pre-booster), Men Y, Pairwise comparison of geometric mean titer.	
Comparison groups	Licensed Polysaccharide Meningococcal Vaccine v MenACWY-CRM Vaccine
Number of subjects included in analysis	98
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	Vaccine Group Ratios
Point estimate	3.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.94
upper limit	6.74

Statistical analysis title	Statistical Analysis 30 for GMT After Booster
Statistical analysis description: Day 1 (Pre-booster), Men Y, Pairwise comparison of geometric mean titer.	
Comparison groups	MenACWY-CRM Vaccine v Meningococcal Naïve

Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	Vaccine Group Ratios
Point estimate	3.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.71
upper limit	6.13

Statistical analysis title	Statistical Analysis 31 for GMT After Booster
Statistical analysis description: Day 8, Men Y, Pairwise comparison of geometric mean titer.	
Comparison groups	Meningococcal Naïve v Licensed Polysaccharide Meningococcal Vaccine
Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	Vaccine Group Ratios
Point estimate	0.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.16
upper limit	0.66

Statistical analysis title	Statistical Analysis 32 for GMT After Booster
Statistical analysis description: Day 8, Men Y, Pairwise comparison of geometric mean titer.	
Comparison groups	Licensed Polysaccharide Meningococcal Vaccine v MenACWY-CRM Vaccine
Number of subjects included in analysis	98
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	Vaccine Group Ratios
Point estimate	121
Confidence interval	
level	95 %
sides	2-sided
lower limit	61
upper limit	241

Statistical analysis title	Statistical Analysis 33 for GMT After Booster
Statistical analysis description: Day 8, Men Y, Pairwise comparison of geometric mean titer.	
Comparison groups	MenACWY-CRM Vaccine v Meningococcal Naïve
Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	Vaccine Group Ratios
Point estimate	40
Confidence interval	
level	95 %
sides	2-sided
lower limit	20
upper limit	80

Statistical analysis title	Statistical Analysis 34 for GMT After Booster
Statistical analysis description: Day 29, Men Y, Pairwise comparison of geometric mean titer.	
Comparison groups	Meningococcal Naïve v Licensed Polysaccharide Meningococcal Vaccine
Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	Vaccine Group Ratios
Point estimate	0.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.32
upper limit	1.05

Statistical analysis title	Statistical Analysis 35 for GMT After Booster
Statistical analysis description: Day 29, Men Y, Pairwise comparison of geometric mean titer.	
Comparison groups	MenACWY-CRM Vaccine v Licensed Polysaccharide Meningococcal Vaccine

Number of subjects included in analysis	98
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	Vaccine Group Ratios
Point estimate	33
Confidence interval	
level	95 %
sides	2-sided
lower limit	18
upper limit	60

Statistical analysis title	Statistical Analysis 36 for GMT After Booster
Statistical analysis description: Day 29, Men Y, Pairwise comparison of geometric mean titer.	
Comparison groups	MenACWY-CRM Vaccine v Meningococcal Naïve
Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	other
Method	ANOVA
Parameter estimate	Vaccine Group Ratios
Point estimate	19
Confidence interval	
level	95 %
sides	2-sided
lower limit	10
upper limit	35

Secondary: 3. Percentages of Subjects With Serum Bactericidal Activity ≥ 4 at 5 Years After Primary Vaccination

End point title	3. Percentages of Subjects With Serum Bactericidal Activity ≥ 4 at 5 Years After Primary Vaccination
End point description: Persistence was measured by percentages of subjects with hSBA ≥ 4 in previously vaccinated subjects and in age-matched meningococcal vaccine naïve subjects. Sera was tested against N. Meningitidis serogroups A, C, W-135 and Y. The analysis was done on the FAS, Antibody Persistence (FAS Persist) Population.	
End point type	Secondary
End point timeframe: Day 1 (5 years after primary vaccination).	

End point values	MenACWY-CRM Vaccine	Licensed Polysaccharide Meningococcal Vaccine	Meningococcal Naïve	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	50	50	53	
Units: Percentages of Subjects				
number (confidence interval 95%)				
Men A	34 (21 to 49)	50 (36 to 64)	23 (12 to 36)	
Men C	84 (71 to 93)	68 (53 to 80)	70 (56 to 82)	
Men W-135	80 (66 to 90)	58 (43 to 72)	55 (40 to 68)	
Men Y	76 (62 to 87)	60 (45 to 74)	60 (46 to 74)	

Statistical analyses

No statistical analyses for this end point

Secondary: 4. Geometric Mean Titer at 5 Years After Primary Vaccination

End point title	4. Geometric Mean Titer at 5 Years After Primary Vaccination
End point description:	
Persistence was measured by hSBA and expressed as hSBA GMT in previously vaccinated subjects and in age-matched meningococcal vaccine naïve subjects. Sera were tested against Neisseria meningitidis serogroups A, C, W-135 and Y.	
The analysis was done on the FAS, Antibody Persistence (FAS Persist) Population.	
End point type	Secondary
End point timeframe:	
Day 1 (5 years after primary vaccination).	

End point values	MenACWY-CRM Vaccine	Licensed Polysaccharide Meningococcal Vaccine	Meningococcal Naïve	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	50	50	53	
Units: Titers				
geometric mean (confidence interval 95%)				
Men A	5.21 (3.51 to 7.74)	7.56 (5.12 to 11)	3 (2.05 to 4.4)	
Men C	20 (12 to 31)	19 (12 to 30)	7.62 (4.86 to 12)	
Men W-135	28 (17 to 46)	12 (7.17 to 20)	11 (6.53 to 17)	
Men Y	27 (17 to 43)	7.67 (4.85 to 12)	9.38 (5.98 to 15)	

Statistical analyses

No statistical analyses for this end point

Secondary: 5. Percentages of Subjects With Serum Bactericidal Activity ≥ 4 After Booster Vaccination

End point title	5. Percentages of Subjects With Serum Bactericidal Activity ≥ 4 After Booster Vaccination
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End point description:

Immunogenicity was measured by hSBA ≥ 4 in previously vaccinated subjects and in age-matched meningococcal vaccine naïve subjects. Sera were tested against *Neisseria meningitidis* serogroups A, C, W-135 and Y.

The analysis was done on the FAS, Immunogenicity after one dose of MenACWY (FAS Booster) Population.

End point type	Secondary
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End point timeframe:

Day 7, Day 28 post booster (5 years after primary vaccination).

End point values	MenACWY-CRM Vaccine	Licensed Polysaccharide Meningococcal Vaccine	Meningococcal Naïve	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	49	49	50	
Units: Percentages of Subjects				
number (confidence interval 95%)				
Day 7 post booster , Men A	100 (93 to 100)	76 (61 to 87)	66 (51 to 79)	
Day 28 post booster, Men A	98 (89 to 100)	94 (83 to 99)	92 (81 to 98)	
Day 7 post booster, Men C	100 (93 to 100)	82 (68 to 91)	94 (83 to 99)	
Day 28 post booster, Men C	100 (93 to 100)	90 (78 to 97)	98 (89 to 100)	
Day 7 post booster, Men W-135	100 (93 to 100)	86 (73 to 94)	92 (81 to 98)	
Day 28 post booster, Men W-135	100 (93 to 100)	94 (83 to 99)	94 (83 to 99)	
Day 7 post booster, Men Y	98 (89 to 100)	78 (63 to 88)	92 (81 to 98)	
Day 28 post booster, Men Y	100 (93 to 100)	100 (93 to 100)	100 (93 to 100)	

Statistical analyses

No statistical analyses for this end point

Secondary: 6. Percentages of Subjects With Serum Bactericidal Activity ≥ 8 After Booster Vaccination

End point title	6. Percentages of Subjects With Serum Bactericidal Activity ≥ 8 After Booster Vaccination
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End point description:

Immunogenicity was measured by serum bactericidal assay with human complement (hSBA) ≥ 8 in previously vaccinated subjects and in age-matched meningococcal vaccine naïve subjects. Sera were tested against *Neisseria meningitidis* serogroups A, C, W-135 and Y.

The analysis was done on the FAS, Immunogenicity after one dose of MenACWY (FAS Booster)

Population.

End point type	Secondary
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End point timeframe:

Day 7, Day 28 post booster (5 years after primary vaccination).

End point values	MenACWY-CRM Vaccine	Licensed Polysaccharide Meningococcal Vaccine	Meningococcal Naïve	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	49	49	50	
Units: Percentages of Subjects				
number (confidence interval 95%)				
Day 7 post booster, Men A	100 (93 to 100)	73 (59 to 85)	64 (49 to 77)	
Day 28 post booster, Men A	98 (89 to 100)	94 (83 to 99)	92 (81 to 98)	
Day 7 post booster, Men C	100 (93 to 100)	78 (63 to 88)	90 (78 to 97)	
Day 28 post booster, Men C	100 (93 to 100)	84 (70 to 93)	98 (89 to 100)	
Day 7 post booster, Men W-135	100 (93 to 100)	84 (70 to 93)	88 (76 to 95)	
Day 28 post booster, Men W-135	100 (93 to 100)	92 (80 to 98)	94 (83 to 99)	
Day 7 post booster, Men Y	98 (89 to 100)	76 (61 to 87)	90 (78 to 97)	
Day 28 post booster, Men Y	100 (93 to 100)	96 (86 to 100)	98 (89 to 100)	

Statistical analyses

No statistical analyses for this end point

Secondary: 7. Geometric Mean Ratio After Booster Vaccination

End point title	7. Geometric Mean Ratio After Booster Vaccination
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End point description:

Ratios are expressed as geometric mean titer at Day 8: Day 1 and at Day 29:Day 1.

The analysis was done on the FAS, Immunogenicity after one dose of MenACWY (FAS Booster)

Population.

End point type	Secondary
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End point timeframe:

Day 8 and Day 29 (at 5 Years After Primary Vaccination).

End point values	MenACWY-CRM Vaccine	Licensed Polysaccharide Meningococcal Vaccine	Meningococcal Naïve	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	49	49	50	
Units: Ratios				
geometric mean (confidence interval 95%)				
Men A (Day 8:1)	205 (113 to 373)	6.1 (3.4 to 11)	11 (6.17 to 20)	
Men A (Day 29:1), N=48, N=49, N=50	155 (92 to 262)	20 (12 to 33)	37 (22 to 62)	
Men C (Day 8:1)	78 (47 to 130)	1.85 (1.13 to 3.03)	9.48 (5.76 to 16)	
Men C (Day 29:1)	60 (37 to 97)	2.64 (1.64 to 4.24)	17 (11 to 28)	
Men W-135 (Day 8:1)	58 (34 to 97)	2.92 (1.75 to 4.87)	5.95 (3.55 to 9.99)	
Men W-135 (Day 29:1)	56 (33 to 95)	4.06 (2.43 to 6.077)	7.48 (4.46 to 13)	
Men Y (Day 8:1), N=48, N=49, N=50	96 (56 to 167)	2.69 (1.58 to 4.58)	7.29 (4.26 to 12)	
Men Y (Day 29:1)	74 (43 to 129)	8.12 (4.73 to 14)	13 (7.3 to 22)	

Statistical analyses

No statistical analyses for this end point

Secondary: 8. Percentages of Subjects With hSBA Seroresponse After Booster Vaccination

End point title	8. Percentages of Subjects With hSBA Seroresponse After Booster Vaccination
End point description: For a subject with hSBA titer <4 at baseline, seroresponse is defined as a post-vaccination hSBA titer ≥8; and for a subject with hSBA titer ≥4 at baseline, seroresponse is defined as a post-vaccination hSBA titer of at least 4 times the baseline. Sera were tested against Neisseria meningitidis serogroups A, C, W-135 and Y. The analysis was done on the FAS, Immunogenicity after one dose of MenACWY (FAS Booster) Population.	
End point type	Secondary
End point timeframe: Day 8, Day 29 (5 years after primary vaccination).	

End point values	MenACWY-CRM Vaccine	Licensed Polysaccharide Meningococcal Vaccine	Meningococcal Naïve	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	49	49	50	
Units: Percentages of Subjects				
number (confidence interval 95%)				

Men A, Day 8	100 (93 to 100)	51 (36 to 66)	60 (45 to 74)	
Men A, Day 29	100 (93 to 100)	76 (61 to 87)	90 (78 to 97)	
Men C, Day 8	96 (86 to 100)	16 (7 to 30)	62 (47 to 75)	
Men C, Day 29	96 (86 to 100)	31 (18 to 45)	80 (66 to 90)	
Men W-135, Day 8	96 (86 to 100)	37 (23 to 52)	48 (34 to 63)	
Men W-135, Day 29	98 (89 to 100)	47 (33 to 62)	58 (43 to 72)	
Men Y, Day 8	94 (83 to 99)	33 (20 to 48)	54 (39 to 68)	
Men Y, Day 29	94 (83 to 99)	55 (40 to 69)	76 (62 to 87)	

Statistical analyses

No statistical analyses for this end point

Secondary: 9. Number of Subjects With at Least One Reactogenicity Sign After Booster Vaccination

End point title	9. Number of Subjects With at Least One Reactogenicity Sign After Booster Vaccination
End point description:	Local and systemic reactions were solicited to assess safety and tolerability of vaccination. The analysis was done on the safety population.
End point type	Secondary
End point timeframe:	Up to Day 7.

End point values	MenACWY-CRM Vaccine	Licensed Polysaccharide Meningococcal Vaccine	Meningococcal Naïve	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	50	50	53	
Units: Number of Subjects				
number (not applicable)				
Local Reactions (any-total)	30	32	40	
Pain (any)	29	27	33	
Erythema (any)	8	8	15	
Induration (any)	5	8	5	
Systemic Reactions (any-total)	31	25	38	
Chills (any)	7	5	3	
Nausea (any)	8	9	11	
Malaise (any)	10	11	15	
Myalgia (any)	16	13	17	
Arthralgia (any)	3	5	6	
Headache (any)	21	17	31	
Fever (≥ 38C) (any)	0	0	1	
Stayed Home (any)	0	2	2	
Analges Antipyr Meds Used (any)	10	8	9	

Statistical analyses

No statistical analyses for this end point

Secondary: 10. Number of Subjects With Unsolicited Adverse Events After Booster Vaccination

End point title	10. Number of Subjects With Unsolicited Adverse Events After Booster Vaccination
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End point description:

Number of subjects with unsolicited Adverse Events (AEs) within 7 days (day 1-7) after the vaccination. The analysis was done on the safety population.

End point type	Secondary
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End point timeframe:

Up to Day 7.

End point values	MenACWY-CRM Vaccine	Licensed Polysaccharide Meningococcal Vaccine	Meningococcal Naïve	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	50	50	53	
Units: Subjects				
Any-Adverse Event	12	7	10	
Ear & Labyrinth Disorders	0	0	1	
Eye Disorders	1	0	1	
Gastrointestinal Disorders	1	1	0	
Gen. Disorders & Admin. Site Cond.	2	3	4	
Infections & Infestations	4	1	2	
Injury & Poisoning	0	1	1	
Musculo., Connect. Tis. & Bone Dis.	4	0	2	
Nervous System Disorders	4	2	4	
Resp., Thoracic & Mediastinal Dis.	0	1	0	
Skin & Subcutaneous Tis. Disorders	2	0	0	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Safety was assessed up to 28 days after vaccination.

Adverse event reporting additional description:

All the AEs reported were solicited post-injection reactions.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	17.1
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Reporting groups

Reporting group title	MenACWY-CRM Vaccine
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Reporting group description:

Subjects had been given one dose of Meningococcal ACWY (MenACWY) vaccine conjugated to CRM197 (cross-reactive material-mutant of diphtheria toxin) 5 years ago.

Reporting group title	Meningococcal Naïve
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Reporting group description:

Subjects were between 16 years to 23 years (age-inclusive) and meningococcal vaccine naïve.

Reporting group title	Licensed Polysaccharide Meningococcal Vaccine
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Reporting group description:

Subjects had been given one dose of licensed Meningococcal (Men ACWY) polysaccharide vaccine (Menomune®) 5 years ago.

Serious adverse events	MenACWY-CRM Vaccine	Meningococcal Naïve	Licensed Polysaccharide Meningococcal Vaccine
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 50 (0.00%)	0 / 53 (0.00%)	0 / 50 (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-CRM Vaccine	Meningococcal Naïve	Licensed Polysaccharide Meningococcal Vaccine
Total subjects affected by non-serious adverse events			
subjects affected / exposed	38 / 50 (76.00%)	46 / 53 (86.79%)	36 / 50 (72.00%)
Nervous system disorders			
Headache			

subjects affected / exposed occurrences (all)	21 / 50 (42.00%) 26	31 / 53 (58.49%) 43	17 / 50 (34.00%) 24
General disorders and administration site conditions			
Chills			
subjects affected / exposed	7 / 50 (14.00%)	3 / 53 (5.66%)	5 / 50 (10.00%)
occurrences (all)	8	4	6
Injection site erythema			
subjects affected / exposed	8 / 50 (16.00%)	15 / 53 (28.30%)	8 / 50 (16.00%)
occurrences (all)	8	15	9
Injection site induration			
subjects affected / exposed	5 / 50 (10.00%)	5 / 53 (9.43%)	8 / 50 (16.00%)
occurrences (all)	5	5	8
Injection site pain			
subjects affected / exposed	29 / 50 (58.00%)	33 / 53 (62.26%)	27 / 50 (54.00%)
occurrences (all)	31	39	28
Malaise			
subjects affected / exposed	10 / 50 (20.00%)	15 / 53 (28.30%)	11 / 50 (22.00%)
occurrences (all)	12	18	12
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	8 / 50 (16.00%)	11 / 53 (20.75%)	9 / 50 (18.00%)
occurrences (all)	8	15	10
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 50 (6.00%)	6 / 53 (11.32%)	5 / 50 (10.00%)
occurrences (all)	4	6	6
Myalgia			
subjects affected / exposed	18 / 50 (36.00%)	18 / 53 (33.96%)	13 / 50 (26.00%)
occurrences (all)	21	25	13

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 January 2010	Update of some analysis collection, physical assessment and study visits procedures.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

N/A

Notes:

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/23114372>