

**Clinical trial results:****Phase 2, Observer Blinded, Controlled, Randomized Multi-Center Study in Adolescents and Young Adults to Evaluate Safety and Immunogenicity of Two Different rMenB with OMV + MenACWY Combination Vaccination Formulations**

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

**Summary**

EudraCT number	2010-023523-23
Trial protocol	PL
Global end of trial date	08 September 2012

**Results information**

Result version number	v2 (current)
This version publication date	04 June 2016
First version publication date	03 May 2015
Version creation reason	<ul style="list-style-type: none"><li>• Correction of full data set re-QC of study needed because of EudraCT system glitch and updates to results are required.</li></ul>

**Trial information****Trial identification**

Sponsor protocol code	V102_03
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**Additional study identifiers**

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01272180
WHO universal trial number (UTN)	-

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)	Yes
EMA paediatric investigation plan number(s)	EMA-000139-PIP01-07
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	17 December 2013
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	08 September 2012
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

1. To demonstrate immunologic noninferiority of 2 doses of 2 different formulations of MenABCWY vaccine to a single dose of MenACWY vaccine, as measured by the percentage of subjects with hSBA seroresponse against *N. meningitidis* serogroups A, C, W-135, and Y, at 30 days after the second vaccination, in healthy adolescents and young adults aged 10 through 25 years.
  2. To identify the optimal formulation of MenABCWY vaccine compared with a single dose of Menveo (MenACWY) and with 2 doses of rMenB+OMV in healthy adolescents and young adults aged 10 through 25 years, based on the overall desirability index.
- The overall desirability index is based on immunogenicity parameters (GMT ratios against *N. meningitidis* serogroups A, C, W-135, and Y and serogroup B test strains at 30 days after the second vaccination) and reactogenicity parameters (percentages of doses associated with severe local and severe systemic solicited AEs following any vaccination).

Protection of trial subjects:

This trial was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki, and that are consistent with Good Clinical Practice (GCP), and the applicable regulatory requirement(s) for the country in which the trial was conducted according to International Conference on Harmonisation (ICH) guidelines, and applicable Standard Operating Procedures (SOPs)..

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	08 August 2011
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	6 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 132
Country: Number of subjects enrolled	United States: 352
Worldwide total number of subjects	484
EEA total number of subjects	132

Notes:

<b>Subjects enrolled per age group</b>	
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)	169
Adolescents (12-17 years)	163
Adults (18-64 years)	152
From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

8 sites in US, 5 sites in Poland

### Pre-assignment

Screening details:

All enrolled subjects were included in the trial

### Period 1

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

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	ABCWY+OMV

Arm description:

Subjects in this group received two doses of ABCWY+OMV combination vaccine, administered two months apart

Arm type	Experimental
Investigational medicinal product name	ABCWY+OMV
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5ml

<b>Arm title</b>	ABCWY+qOMV
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Arm description:

Subjects in this group received two doses of ABCWY+qOMV combination vaccine, administered two months apart

Arm type	Experimental
Investigational medicinal product name	ABCWY+qOMV
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5ml

<b>Arm title</b>	rMenB +OMV
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Arm description:

Subjects in this group received two doses of rMenB + OMV vaccine, administered two months apart

Arm type	Active comparator
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Investigational medicinal product name	rMenB+OMV
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use
Dosage and administration details:	
0.5ml	
<b>Arm title</b>	PBO/ACWY

Arm description:

Subjects in this group received one dose of placebo followed by one dose of MenACWY vaccine two months later.

Arm type	Active comparator
Investigational medicinal product name	PBO/ACWY
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5ml

<b>Number of subjects in period 1</b>	ABCWY+OMV	ABCWY+qOMV	rMenB +OMV
Started	120	121	122
Completed	103	100	109
Not completed	17	21	13
Consent withdrawn by subject	2	6	3
Adverse event, non-fatal	-	-	1
Inappropriate enrollment	-	-	1
Lost to follow-up	15	14	8
Protocol deviation	-	1	-

<b>Number of subjects in period 1</b>	PBO/ACWY
Started	121
Completed	107
Not completed	14
Consent withdrawn by subject	2
Adverse event, non-fatal	-
Inappropriate enrollment	1
Lost to follow-up	10
Protocol deviation	1

## Baseline characteristics

### Reporting groups

Reporting group title	ABCWY+OMV
Reporting group description:	
Subjects in this group received two doses of ABCWY+OMV combination vaccine, administered two months apart	
Reporting group title	ABCWY+qOMV
Reporting group description:	
Subjects in this group received two doses of ABCWY+qOMV combination vaccine, administered two months apart	
Reporting group title	rMenB +OMV
Reporting group description:	
Subjects in this group received two doses of rMenB + OMV vaccine,administered two months apart	
Reporting group title	PBO/ACWY
Reporting group description:	
Subjects in this group received one dose of placebo followed by one dose of MenACWY vaccine two months later.	

Reporting group values	ABCWY+OMV	ABCWY+qOMV	rMenB +OMV
Number of subjects	120	121	122
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	14.7	15.1	15.3
standard deviation	± 4.7	± 4.9	± 4.9
Gender categorical Units: Subjects			
Female	61	68	60
Male	59	53	62

Reporting group values	PBO/ACWY	Total	
Number of subjects	121	484	
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days)		0 0 0	

Infants and toddlers (28 days-23 months)		0	
Children (2-11 years)		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	15		
standard deviation	± 5.1	-	
Gender categorical			
Units: Subjects			
Female	64	253	
Male	57	231	

## End points

### End points reporting groups

Reporting group title	ABCWY+OMV
Reporting group description: Subjects in this group received two doses of ABCWY+OMV combination vaccine, administered two months apart	
Reporting group title	ABCWY+qOMV
Reporting group description: Subjects in this group received two doses of ABCWY+qOMV combination vaccine, administered two months apart	
Reporting group title	rMenB +OMV
Reporting group description: Subjects in this group received two doses of rMenB + OMV vaccine, administered two months apart	
Reporting group title	PBO/ACWY
Reporting group description: Subjects in this group received one dose of placebo followed by one dose of MenACWY vaccine two months later.	

### Primary: 1.Percentages of Subjects With a Seroresponse Against N.Meningitidis Serogroups A,C,W-135,Y, After Receiving Different Formulations of MenABCWY Combination Vaccine.

End point title	1.Percentages of Subjects With a Seroresponse Against N.Meningitidis Serogroups A,C,W-135,Y, After Receiving Different Formulations of MenABCWY Combination Vaccine. <sup>[1]</sup>
End point description: Non-inferiority of immune response of two doses of two different formulations of MenABCWY vaccine to a single dose of MenACWY vaccine as measured by the percentage of subjects with hSBA seroresponse against N.meningitidis serogroups A,C,W and Y. Seroresponse is defined as: 1. For subjects with a pre-vaccination hSBA titer < 1:4, a post-vaccination hSBA titer ≥ 1:8; 2. For subjects with a pre-vaccination hSBA titer ≥ 1:4, an increase in hSBA titer of at least four times the prevaccination titer. Functional bactericidal antibodies directed against serogroups A,C,W,Y meningococci were measured with a serum bactericidal activity assay using human serum as the source of exogenous complement (hSBA).	
End point type	Primary
End point timeframe: One month after the second vaccination (Day 91)	

#### Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.  
Justification: No statistical analysis is associated to this endpoint.

End point values	ABCWY+OMV	ABCWY+qOMV	PBO/ACWY	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	90	85	76	
Units: Percentages of subjects				
number (confidence interval 95%)				
Men A (N=88, 83, 75)	90 (81 to 95)	92 (83 to 97)	73 (62 to 83)	
Men C (N=86, 84, 76)	95 (89 to 99)	93 (85 to 97)	63 (51 to 74)	
Men W-135 (N=75, 73, 60)	80 (69 to 88)	84 (73 to 91)	65 (52 to 77)	



Men Y (N=65, 70, 59)	92 (83 to 97)	90 (80 to 96)	75 (62 to 85)	
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## Statistical analyses

<b>Statistical analysis title</b>	Non-inferiority seroresponse against N.meningitis
Statistical analysis description:	
Non-inferiority of seroresponse against N.meningitidis serogroup A of two doses of MenABCWY combination vaccine to that of one dose of MenACWY vaccine	
Comparison groups	ABCWY+OMV v PBO/ACWY
Number of subjects included in analysis	166
Analysis specification	Pre-specified
Analysis type	non-inferiority <sup>[2]</sup>
Method	Miettinen and Nurminen
Parameter estimate	Group Difference % (ABCWY+OMV -ACWY)
Point estimate	16
Confidence interval	
level	95 %
sides	2-sided
lower limit	5
upper limit	29

Notes:

[2] - The immune response of ABCWY+OMV group was considered to be non-inferior to that of PBO/ACWY group if the lower limit of the two-sided 95% confidence interval of the difference between groups in percentage of subjects with seroresponse is greater than -10% for each of A, C, W-135 and Y serogroups, at 30 days after the last vaccination

<b>Statistical analysis title</b>	Non-inferiority seroresponse against N.meningitis
Statistical analysis description:	
Non-inferiority of seroresponse against N.meningitidis serogroup C of two doses of MenABCWY combination vaccine to that of one dose of MenACWY vaccine	
Comparison groups	ABCWY+OMV v PBO/ACWY
Number of subjects included in analysis	166
Analysis specification	Pre-specified
Analysis type	non-inferiority <sup>[3]</sup>
Method	Miettinen and Nurminen
Parameter estimate	Group Difference % (ABCWY+OMV -ACWY)
Point estimate	32
Confidence interval	
level	95 %
sides	2-sided
lower limit	21
upper limit	44

Notes:

[3] - The immune response of ABCWY+OMV group was considered to be non-inferior to that of PBO/ACWY group if the lower limit of the two-sided 95% confidence interval of the difference between groups in percentage of subjects with seroresponse is greater than -10% for each of A, C, W-135 and Y serogroups, at 30 days after the last vaccination

<b>Statistical analysis title</b>	Non-inferiority seroresponse against N.meningitis
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**Statistical analysis description:**

Non-inferiority of seroresponse against N.meningitidis serogroup W-135 of two doses of MenABCWY combination vaccine to that of one dose of MenACWY vaccine

Comparison groups	ABCWY+OMV v PBO/ACWY
Number of subjects included in analysis	166
Analysis specification	Pre-specified
Analysis type	non-inferiority <sup>[4]</sup>
Method	Miettinen and Nurminen
Parameter estimate	Group Difference % (ABCWY+OMV -ACWY)
Point estimate	15
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	30

**Notes:**

[4] - The immune response of ABCWY+OMV group was considered to be non-inferior to that of PBO/ACWY group if the lower limit of the two-sided 95% confidence interval of the difference between groups in percentage of subjects with seroresponse is greater than -10% for each of A, C, W-135 and Y serogroups, at 30 days after the last vaccination.

<b>Statistical analysis title</b>	Non-inferiority seroresponse against N.meningitis
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**Statistical analysis description:**

Non-inferiority of seroresponse against N.meningitidis serogroup Y of two doses of MenABCWY combination vaccine to that of one dose of MenACWY vaccine

Comparison groups	ABCWY+OMV v PBO/ACWY
Number of subjects included in analysis	166
Analysis specification	Pre-specified
Analysis type	non-inferiority <sup>[5]</sup>
Method	Miettinen and Nurminen
Parameter estimate	Group Difference % (ABCWY+OMV -ACWY)
Point estimate	18
Confidence interval	
level	95 %
sides	2-sided
lower limit	5
upper limit	31

**Notes:**

[5] - The immune response of ABCWY+OMV group was considered to be non-inferior to that of PBO/ACWY group if the lower limit of the two-sided 95% confidence interval of the difference between groups in percentage of subjects with seroresponse is greater than -10% for each of A, C, W-135 and Y serogroups, at 30 days after the last vaccination.

<b>Statistical analysis title</b>	Non-inferiority seroresponse against N.meningitis
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**Statistical analysis description:**

Non-inferiority of seroresponse against N.meningitidis serogroup A of two doses of MenABCWY combination vaccine to that of one dose of MenACWY vaccine

Comparison groups	ABCWY+qOMV v PBO/ACWY
Number of subjects included in analysis	161
Analysis specification	Pre-specified
Analysis type	non-inferiority <sup>[6]</sup>
Method	Miettinen and Nurminen
Parameter estimate	Group Difference % (ABCWY+OMV -ACWY)
Point estimate	18

Confidence interval	
level	95 %
sides	2-sided
lower limit	7
upper limit	30

Notes:

[6] - The immune response of ABCWY+qOMV group was considered to be non-inferior to that of PBO/ACWY group if the lower limit of the two-sided 95% confidence interval of the difference between groups in percentage of subjects with seroresponse is greater than -10% for each of A, C, W-135 and Y serogroups, at 30 days after the last vaccination.

<b>Statistical analysis title</b>	Non-inferiority seroresponse against N.meningitis
Statistical analysis description:	
Non-inferiority of seroresponse against N.meningitidis serogroup C of two doses of MenABCWY combination vaccine to that of one dose of MenACWY vaccine	
Comparison groups	ABCWY+qOMV v PBO/ACWY
Number of subjects included in analysis	161
Analysis specification	Pre-specified
Analysis type	non-inferiority <sup>[7]</sup>
Method	Miettinen and Nurminen
Parameter estimate	Group Difference % (ABCWY+OMV -ACWY)
Point estimate	30
Confidence interval	
level	95 %
sides	2-sided
lower limit	18
upper limit	42

Notes:

[7] - The immune response of ABCWY+qOMV group was considered to be non-inferior to that of PBO/ACWY group if the lower limit of the two-sided 95% confidence interval of the difference between groups in percentage of subjects with seroresponse is greater than -10% for each of A, C, W-135 and Y serogroups, at 30 days after the last vaccination.

<b>Statistical analysis title</b>	Non-inferiority seroresponse against N.meningitis
Statistical analysis description:	
Non-inferiority of seroresponse against N.meningitidis serogroup W of two doses of MenABCWY combination vaccine to that of one dose of MenACWY vaccine	
Comparison groups	ABCWY+qOMV v PBO/ACWY
Number of subjects included in analysis	161
Analysis specification	Pre-specified
Analysis type	non-inferiority <sup>[8]</sup>
Method	Miettinen and Nurminen
Parameter estimate	Group Difference % (ABCWY+OMV -ACWY)
Point estimate	19
Confidence interval	
level	95 %
sides	2-sided
lower limit	4
upper limit	33

Notes:

[8] - The immune response of ABCWY+qOMV group was considered to be non-inferior to that of PBO/ACWY group if the lower limit of the two-sided 95% confidence interval of the difference between groups in percentage of subjects with seroresponse is greater than -10% for each of A, C, W-135 and Y serogroups, at 30 days after the last vaccination

	Non-inferiority seroresponse against N.meningitis
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<b>Statistical analysis title</b>	
Statistical analysis description: Non-inferiority of seroresponse against N.meningitidis serogroup Y of two doses of MenABCWY combination vaccine to that of one dose of MenACWY vaccine	
Comparison groups	ABCWY+qOMV v PBO/ACWY
Number of subjects included in analysis	161
Analysis specification	Pre-specified
Analysis type	non-inferiority <sup>[9]</sup>
Method	Miettinen and Nurminen
Parameter estimate	Group Difference % (ABCWY+OMV -ACWY)
Point estimate	15
Confidence interval	
level	95 %
sides	2-sided
lower limit	3
upper limit	29

Notes:

[9] - The immune response of ABCWY+qOMV group was considered to be non-inferior to that of PBO/ACWY group if the lower limit of the two-sided 95% confidence interval of the difference between groups in percentage of subjects with seroresponse is greater than -10% for each of A, C, W-135 and Y serogroups, at 30 days after the last vaccination.

### **Primary: 2.Desirability Index for Each Vaccine Group, Based on Immunogenicity and Reactogenicity Parameters**

End point title	2.Desirability Index for Each Vaccine Group, Based on Immunogenicity and Reactogenicity Parameters <sup>[10][11]</sup>
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End point description:

The overall desirability index (DI) used to identify the optimal formulation of the combination vaccine was based on immunogenicity and reactogenicity parameters (on a scale of 0 to 1, with 0 for an undesirable response and 1 for a highly desirable response) as follows: Between-group ratios of hSBA GMTs were calculated, adjusted for prevaccination titer and center, against serogroups A, C, W, and Y (ABCWY+OMV group or ABCWY+qOMV group vs. Placebo/ACWY group) and against the 4 serogroup B test strains (ABCWY+OMV group or ABCWY+qOMV group vs. rMenB+OMV group). Reactogenicity was measured by the percentage of doses associated with severe local and systemic solicited AEs within 3 days following vaccination. Each immunogenicity and reactogenicity endpoint was assigned its own DI based on predefined desirability functions. The overall DI was calculated using the weighted geometric mean of the DI values of each of the ten parameters to derive an overall DI for each formulation

End point type	Primary
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End point timeframe:

One month after the second vaccination (Day 91)

Notes:

[10] - 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.

[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: No statistical analysis is associated to this endpoint.

<b>End point values</b>	ABCWY+OMV	ABCWY+qOMV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	86	82		
Units: Ratio				
number (not applicable)				
Desirability index (50/50 Immuno/ Reactogenicity)	0.306	0.325		

## Statistical analyses

No statistical analyses for this end point

### Secondary: 3. Percentages of Subjects With hSBA Titers $\geq 1:8$ Against N.Meningitidis Serogroups A,C,W-135 and Y, After Vaccination With Different Formulations of MenABCWY Combination Vaccine.

End point title	3. Percentages of Subjects With hSBA Titers $\geq 1:8$ Against N.Meningitidis Serogroups A,C,W-135 and Y, After Vaccination With Different Formulations of MenABCWY Combination Vaccine. <sup>[12]</sup>
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End point description:

Percentages of subjects with hSBA titers  $\geq 1:8$  against N.meningitidis serogroups A,C,W-135 and Y, after two doses of either ABCWY+OMV or ABCWY+qOMV combination vaccine or one dose of MenACWY vaccine.

End point type	Secondary
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End point timeframe:

Day 1 and one month after second vaccination (Day 91)

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No statistical analysis is associated to this endpoint.

End point values	ABCWY+OMV	ABCWY+qOMV	PBO/ACWY	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	90	85	76	
Units: Percentages of subjects				
number (confidence interval 95%)				
Men A (Day 1; N=90, 85, 76)	8 (3 to 15)	6 (2 to 13)	1 (0.033 to 7)	
Men A (Day 91; N=88, 83, 75)	93 (86 to 97)	95 (88 to 99)	73 (62 to 83)	
Men C (Day 1; N=88, 85, 76)	35 (25 to 46)	35 (25 to 46)	32 (21 to 43)	
Men C (Day 91; N=86, 84, 76)	99 (94 to 100)	100 (96 to 100)	83 (73 to 91)	
Men W-135 (Day 1; N=86, 79, 68)	66 (55 to 76)	58 (47 to 69)	51 (39 to 64)	
Men W-135 (Day 91; N=77, 75, 65)	100 (95 to 100)	100 (95 to 100)	89 (79 to 96)	
Men Y (Day 1; N=89, 85, 74)	18 (11 to 28)	15 (8 to 25)	8 (3 to 17)	
Men Y (Day 91; N=65, 70, 60)	97 (89 to 100)	97 (90 to 100)	82 (70 to 90)	

## Statistical analyses

No statistical analyses for this end point

### Secondary: 4. The hSBA GMTs Against N.Meningitidis Serogroups A,C,W-135 and Y,

**After Vaccination With Different Formulations of MenABCWY Combination Vaccine.**

End point title	4. The hSBA GMTs Against N.Meningitidis Serogroups A,C,W-135 and Y, After Vaccination With Different Formulations of MenABCWY Combination Vaccine. <sup>[13]</sup>
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End point description:

The hSBA GMTs against N.meningitidis serogroups A,C,W-135 and Y, after two doses of either ABCWY+OMV or ABCWY+qOMV combination vaccine, or one dose of MenACWY vaccine.

End point type	Secondary
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End point timeframe:

Day 1 and one month after the second vaccination (Day 91)

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No statistical analysis is associated to this endpoint.

End point values	ABCWY+OMV	ABCWY+qOMV	PBO/ACWY	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	90	85	76	
Units: Titers				
geometric mean (confidence interval 95%)				
Men A (Day 1; N=90, 85, 76)	1.57 (1.28 to 1.92)	1.32 (1.07 to 1.63)	1.33 (1.08 to 1.65)	
Men A (Day 91; N=88, 83,75)	71 (49 to 102)	77 (53 to 111)	45 (31 to 65)	
Men C (Day 1; N=88, 85,76)	4.15 (3.02 to 5.69)	3.72 (2.69 to 5.12)	3.93 (2.84 to 5.45)	
Men C (Day 91; N=86, 84, 76)	214 (148 to 309)	187 (129 to 272)	55 (38 to 80)	
Men W-135 (Day 1; N=86,79, 68)	14 (8.88 to 22)	10 (6.45 to 16)	6.58 (4.11 to 11)	
Men W-135 (Day 91;N=77, 75, 65)	239 (178 to 322)	288 (214 to 389)	65 (48 to 90)	
Men Y (Day 1; N=89, 85,74)	2.01 (1.52 to 2.66)	1.91 (1.43 to 2.53)	1.52 (1.14 to 2.04)	
Men Y (Day 91; N=65, 70,60)	149 (95 to 234)	129 (83 to 201)	46 (29 to 72)	

**Statistical analyses**

No statistical analyses for this end point

**Secondary: 5. Percentages of Subjects With hSBA Titers  $\geq 1:5$  and  $\geq 1:8$  Against N.Meningitidis Serogroup B Test Strains, After Vaccination With Different Formulations of MenABCWY Combination Vaccine**

End point title	5. Percentages of Subjects With hSBA Titers $\geq 1:5$ and $\geq 1:8$ Against N.Meningitidis Serogroup B Test Strains, After Vaccination With Different Formulations of MenABCWY Combination Vaccine <sup>[14]</sup>
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End point description:

The percentages of subjects with hSBA titers  $\geq 1:5$  and  $\geq 1:8$  against four different strains of N.meningitidis serogroup B, after two doses of ABCWY+OMV, ABCWY+qOMV or rMenB+OMV vaccine.

End point type	Secondary
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End point timeframe:

Day 1 and one month after the second vaccination (Day 91)

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No statistical analysis is associated to this endpoint.

End point values	ABCWY+OMV	ABCWY+qOMV	rMenB +OMV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	90	85	92	
Units: Percentages of subjects				
number (confidence interval 95%)				
M14459 (Day 1; hSBA $\geq 1:5$ ; N=90, 85, 92)	9 (4 to 17)	4 (1 to 10)	5 (2 to 12)	
M14459 (Day 91; hSBA $\geq 1:5$ ; N=89, 85, 92)	64 (53 to 74)	71 (60 to 80)	82 (72 to 89)	
M07-0241084 (Day 1; hSBA $\geq 1:5$ ; N=89, 84, 92)	26 (17 to 36)	27 (18 to 38)	23 (15 to 33)	
M07-0241084 (Day 91; hSBA $\geq 1:5$ ; N=88, 85, 92)	64 (53 to 74)	55 (44 to 66)	73 (63 to 82)	
M01-0240364 (Day 1; hSBA $\geq 1:5$ ; N=90, 84, 91)	3 (1 to 9)	14 (8 to 24)	4 (1 to 11)	
M01-0240364 (Day 91; hSBA $\geq 1:5$ ; N=86, 84, 90)	80 (70 to 88)	80 (70 to 88)	93 (86 to 98)	
NZ 98/254 (Day 1; hSBA $\geq 1:5$ ; N=89, 85, 92)	3 (1 to 10)	1 (0 to 6)	3 (1 to 9)	
NZ 98/254 (Day 91; hSBA $\geq 1:5$ ; N=89, 84, 92)	62 (51 to 72)	56 (45 to 67)	88 (80 to 94)	
M14459 (Day 1; hSBA $\geq 1:8$ ; N=90, 85, 92)	6 (2 to 12)	2 (0 to 8)	4 (1 to 11)	
M14459 (Day 91; hSBA $\geq 1:8$ ; N=89, 85, 92)	58 (47 to 69)	66 (55 to 76)	77 (67 to 85)	
M07-0241084 (Day 1; hSBA $\geq 1:8$ ; N=89, 84, 92)	18 (11 to 28)	20 (12 to 30)	14 (8 to 23)	
M07-0241084 (Day 91; hSBA $\geq 1:8$ ; N=88, 85, 92)	49 (38 to 60)	47 (36 to 58)	60 (49 to 70)	
M01-0240364 (Day 1; hSBA $\geq 1:8$ ; N=90, 84, 91)	2 (0 to 8)	13 (7 to 22)	4 (1 to 11)	
M01-0240364 (Day 91; hSBA $\geq 1:8$ ; N=86, 84, 90)	79 (69 to 87)	79 (68 to 87)	91 (83 to 96)	
NZ 98/254 (Day 1; hSBA $\geq 8$ ; N=89, 85, 92)	3 (1 to 10)	0 (0 to 4)	3 (1 to 9)	
NZ 98/254 (Day 91; hSBA $\geq 1:8$ ; N=89, 84, 92)	47 (37 to 58)	49 (38 to 60)	77 (67 to 85)	

## Statistical analyses

No statistical analyses for this end point

## Secondary: 6.Percentages of Subjects With at Least 4-fold Increase in hSBA Titers Against N.Meningitidis Serogroup B Test Strains, After Vaccination With Different Formulations of MenABCWY Combination Vaccine.

End point title	6.Percentages of Subjects With at Least 4-fold Increase in hSBA Titers Against N.Meningitidis Serogroup B Test Strains, After Vaccination With Different Formulations of MenABCWY
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## End point description:

The percentages of subjects with at least 4-fold increase in hSBA titers against four different strains of N.meningitidis serogroup B, after two doses of ABCWY+OMV, ABCWY+qOMV or rMenB+OMV vaccine 4-fold increase is defined as follows;  
for subjects with a prevaccination hSBA < 1:2, a postvaccination hSBA ≥ 1:8, for subjects with a prevaccination hSBA ≥ 1:2, at least a 4-fold increase

## End point type

Secondary

## End point timeframe:

One month after the second vaccination (Day 91)

## Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No statistical analysis is associated to this endpoint.

End point values	ABCWY+OMV	ABCWY+qOMV	rMenB +OMV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	90	85	92	
Units: Percentages of subjects				
number (confidence interval 95%)				
M14459 (N=89, 85, 92)	56 (45 to 67)	62 (51 to 73)	75 (65 to 83)	
M07-0241084 (N=87, 84,92)	28 (19 to 38)	25 (16 to 36)	42 (32 to 53)	
M01-0240364 (N=86, 83, 89)	79 (69 to 87)	70 (59 to 79)	88 (79 to 94)	
NZ98/254 (N=88, 84, 92)	47 (36 to 58)	48 (37 to 59)	76 (66 to 84)	

## Statistical analyses

No statistical analyses for this end point

**Secondary: 7. The hSBA GMTs Against N.Meningitidis serogroup B Test Strains, After Vaccination With Different Formulations of MenABCWY Combination Vaccine.**

## End point title

7. The hSBA GMTs Against N.Meningitidis serogroup B Test Strains, After Vaccination With Different Formulations of MenABCWY Combination Vaccine.<sup>[16]</sup>

## End point description:

The hSBA GMTs against N.meningitidis serogroup B test strains after two doses of ABCWY+OMV, ABCWY+qOMV or rMenB+OMV vaccine.

## End point type

Secondary

## End point timeframe:

Day 1 and one month after the second vaccination (Day 91)

## Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No statistical analysis is associated to this endpoint.



End point values	ABCWY+OMV	ABCWY+qOMV	rMenB +OMV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	90	85	92	
Units: Titers				
geometric mean (confidence interval 95%)				
M14459 (Day 1; N=90,85,92)	1.32 (1.09 to 1.59)	1.15 (0.95 to 1.4)	1.26 (1.04 to 1.53)	
M14459 (Day 91; N= 89, 85, 92)	9.24 (6.19 to 14)	11 (7.51 to 17)	17 (11 to 25)	
M07-0241084 (Day 1; N= 89, 84, 92)	2.55 (1.86 to 3.49)	2.45 (1.76 to 3.4)	2.13 (1.54 to 2.94)	
M07-0241084 (Day 91; N= 88, 85, 92)	7.24 (5.4 to 9.71)	6.26 (4.63 to 8.46)	12 (8.83 to 16)	
M01-0240364 (Day 1; N=90, 84, 91)	1.08 (0.82 to 1.42)	1.72 (1.29 to 2.28)	1.14 (0.86 to 1.51)	
M01-0240364 (Day 91; N= 86, 84, 90)	55 (33 to 93)	48 (28 to 83)	118 (69 to 202)	
NZ 98/254 (Day 1; N= 89, 85, 92)	1.2 (1.03 to 1.39)	1.1 (0.94 to 1.28)	1.21 (1.04 to 1.42)	
NZ 98/254 (Day 91; N= 89, 84, 92)	8.68 (5.91 to 13)	7.88 (5.3 to 12)	19 (13 to 27)	

## Statistical analyses

No statistical analyses for this end point

## Secondary: 8. The Geometric Mean Ratio of Post vs Pre Vaccination GMTs Against N.Meningitidis Serogroup B Test Strains, After Vaccination With Different Formulations of MenABCWY Combination Vaccine

End point title	8. The Geometric Mean Ratio of Post vs Pre Vaccination GMTs Against N.Meningitidis Serogroup B Test Strains, After Vaccination With Different Formulations of MenABCWY Combination Vaccine <sup>[17]</sup>
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End point description:

The geometric mean ratio (GMR) of post vaccination versus pre vaccination GMTs against N.meningitidis serogroup B test strains after two doses of ABCWY+OMV, ABCWY+qOMV or rMenB+OMV vaccine.

End point type	Secondary
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End point timeframe:

One month after the second vaccination/prevaccination (Day 91/day 1)

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No statistical analysis is associated to this endpoint.

End point values	ABCWY+OMV	ABCWY+qOMV	rMenB +OMV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	90	85	92	
Units: Ratio				
geometric mean (confidence interval 95%)				
M14459 (N=89, 85, 92)	7.32 (4.89 to 11)	9.41 (6.19 to 14)	14 (9.01 to 21)	

M07-0241084 (N=87,84,92)	2.94 (2.15 to 4.02)	2.59 (1.88 to 3.58)	5.16 (3.76 to 7.08)	
M01-0240364 (N=86, 83, 89)	48 (27 to 83)	30 (17 to 54)	98 (56 to 173)	
NZ98/254 (N=88,84,92)	7.44 (5.06 to 11)	6.91 (4.64 to 10)	16 (11 to 23)	

## Statistical analyses

No statistical analyses for this end point

## Secondary: 9. Number of Subjects Reporting Solicited Adverse Events After Receiving Any Vaccination in This Study

End point title	9. Number of Subjects Reporting Solicited Adverse Events After Receiving Any Vaccination in This Study
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End point description:

The number of subjects reporting solicited local and systemic adverse events and other indicators of reactogenicity after vaccination with ABCWY+OMV, ABCWY+qOMV or rMenB+OMV or MenACWY

End point type	Secondary
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End point timeframe:

Day 1 through day 7 after any vaccination

End point values	ABCWY+OMV	ABCWY+qOMV	rMenB +OMV	PBO/ACWY
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	120	120	120	109
Units: Subjects				
Erythema (N=107, 110, 115, 99)	0	1	0	2
Induration (N=107, 110, 115, 99)	1	0	0	2
Pain (N=108, 110, 115, 99)	29	29	44	9
Chills (N=108, 110, 115, 99)	2	4	1	0
Myalgia(N=108, 110, 115, 99)	16	13	24	4
Arthralgia(N=108, 110, 115, 99)	4	5	4	0
Headache (N=108, 110, 115, 99)	6	4	10	4
Fatigue (N=108, 110, 115, 99)	4	9	9	2
Nausea(N=108, 110, 115, 99)	2	5	7	0
Rash (N=108, 110, 115, 99)	2	3	2	4
Loss of appetite (N=108, 110, 115, 99)	3	4	3	0
Fever ( >= 38C ) (N=108, 111, 115, 99)	7	5	6	1
Medically attended fever (N=108, 110, 115, 99)	2	0	0	0
Prophylactic use antipyretic (N=108, 110, 115, 99)	17	14	16	7
Therapeutic use antipyretic (N=108, 110, 115, 99)	18	26	27	10

## Statistical analyses

No statistical analyses for this end point

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**Secondary: 10. The Number of Subjects Reporting Unsolicited Adverse Events After Receiving Any Vaccination in This Study**

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End point title	10. The Number of Subjects Reporting Unsolicited Adverse Events After Receiving Any Vaccination in This Study
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End point description:

The number of subjects reporting unsolicited AEs after vaccination with ABCWY+OMV, ABCWY+qOMV, rMenB+OMV or MenACWY

End point type	Secondary
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End point timeframe:

Throughout the study ( Day 1 to Day 241)

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End point values	ABCWY+OMV	ABCWY+qOMV	rMenB +OMV	PBO/ACWY
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	120	120	120	109
Units: Subjects				
Any AE within 30days first vaccination (days 1-30)	21	28	33	20
Any AE within 30days second vaccination(day 61-91)	9	5	9	7
Any AE from days 1-91	51	55	66	50
Any AE from days 1-241	56	60	71	60
Medically attended AEs from days 92-241	26	24	30	31
SAEs (days 1-241)	2	2	1	3
AEs leading to premature withdrawal (days 1-241)	0	0	2	0
Deaths (days 1-241)	0	0	0	0

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**Statistical analyses**

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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; unsolicited AEs and SAEs were collected throughout the study period (Day 1 to Day 241)

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	ABCWY+OMV
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Reporting group description:

Subjects in this group received two doses of ABCWY+OMV combination vaccine, administered two months apart

Reporting group title	ABCWY+qOMV
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Reporting group description:

Subjects in this group received two doses of ABCWY+qOMV combination vaccine, administered two months apart

Reporting group title	rMenB +OMV
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Reporting group description:

Subjects in this group received two doses of rMenB + OMV vaccine, administered two months apart

Reporting group title	PBO/ACWY
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Reporting group description:

Subjects in this group received one dose of placebo followed by one dose of MenACWY vaccine two months later.

Serious adverse events	ABCWY+OMV	ABCWY+qOMV	rMenB +OMV
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 119 (1.68%)	2 / 121 (1.65%)	1 / 121 (0.83%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Nervous system disorders			
Convulsion			
subjects affected / exposed	0 / 119 (0.00%)	0 / 121 (0.00%)	1 / 121 (0.83%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	0 / 119 (0.00%)	0 / 121 (0.00%)	0 / 121 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast			

disorders			
Spermatocele			
subjects affected / exposed	0 / 119 (0.00%)	0 / 121 (0.00%)	0 / 121 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Sleep Apnoea syndrome			
subjects affected / exposed	0 / 119 (0.00%)	0 / 121 (0.00%)	0 / 121 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Abnormal behaviour			
subjects affected / exposed	0 / 119 (0.00%)	1 / 121 (0.83%)	0 / 121 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	1 / 119 (0.84%)	0 / 121 (0.00%)	0 / 121 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pertussis			
subjects affected / exposed	0 / 119 (0.00%)	1 / 121 (0.83%)	0 / 121 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 119 (0.84%)	0 / 121 (0.00%)	0 / 121 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 119 (0.00%)	1 / 121 (0.83%)	0 / 121 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

<b>Serious adverse events</b>	PBO/ACWY		
Total subjects affected by serious adverse events			

subjects affected / exposed	3 / 108 (2.78%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Nervous system disorders			
Convulsion			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Spermatocele			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Sleep Apnoea syndrome			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Abnormal behaviour			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pertussis			

subjects affected / exposed	0 / 108 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	0 / 108 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

<b>Non-serious adverse events</b>	ABCWY+OMV	ABCWY+qOMV	rMenB +OMV
Total subjects affected by non-serious adverse events			
subjects affected / exposed	104 / 119 (87.39%)	104 / 121 (85.95%)	110 / 121 (90.91%)
Nervous system disorders			
Headache			
subjects affected / exposed	38 / 119 (31.93%)	41 / 121 (33.88%)	53 / 121 (43.80%)
occurrences (all)	57	71	100
General disorders and administration site conditions			
Chills			
subjects affected / exposed	19 / 119 (15.97%)	22 / 121 (18.18%)	29 / 121 (23.97%)
occurrences (all)	22	29	43
Fatigue			
subjects affected / exposed	33 / 119 (27.73%)	47 / 121 (38.84%)	51 / 121 (42.15%)
occurrences (all)	52	80	91
Injection Site Erythema			
subjects affected / exposed	59 / 119 (49.58%)	53 / 121 (43.80%)	71 / 121 (58.68%)
occurrences (all)	92	74	108
Injection Site Induration			
subjects affected / exposed	47 / 119 (39.50%)	52 / 121 (42.98%)	45 / 121 (37.19%)
occurrences (all)	74	78	68
Injection Site Pain			

subjects affected / exposed occurrences (all)	100 / 119 (84.03%) 187	97 / 121 (80.17%) 180	106 / 121 (87.60%) 208
Pyrexia subjects affected / exposed occurrences (all)	14 / 119 (11.76%) 16	8 / 121 (6.61%) 9	7 / 121 (5.79%) 8
Gastrointestinal disorders			
Diarrhoea subjects affected / exposed occurrences (all)	4 / 119 (3.36%) 4	2 / 121 (1.65%) 2	2 / 121 (1.65%) 2
Nausea subjects affected / exposed occurrences (all)	15 / 119 (12.61%) 23	25 / 121 (20.66%) 28	30 / 121 (24.79%) 50
Respiratory, thoracic and mediastinal disorders			
Rhinitis Allergic subjects affected / exposed occurrences (all)	5 / 119 (4.20%) 5	4 / 121 (3.31%) 4	3 / 121 (2.48%) 3
Skin and subcutaneous tissue disorders			
Rash subjects affected / exposed occurrences (all)	6 / 119 (5.04%) 7	9 / 121 (7.44%) 11	4 / 121 (3.31%) 5
Musculoskeletal and connective tissue disorders			
Arthralgia subjects affected / exposed occurrences (all)	22 / 119 (18.49%) 28	24 / 121 (19.83%) 30	25 / 121 (20.66%) 39
Myalgia subjects affected / exposed occurrences (all)	65 / 119 (54.62%) 109	67 / 121 (55.37%) 104	66 / 121 (54.55%) 117
Infections and infestations			
Nasopharyngitis subjects affected / exposed occurrences (all)	3 / 119 (2.52%) 3	8 / 121 (6.61%) 8	6 / 121 (4.96%) 8
Otitis Media Acute subjects affected / exposed occurrences (all)	2 / 119 (1.68%) 2	0 / 121 (0.00%) 0	2 / 121 (1.65%) 2
Pharyngitis			



subjects affected / exposed occurrences (all)	7 / 119 (5.88%) 8	8 / 121 (6.61%) 10	7 / 121 (5.79%) 7
Pharyngitis Stretococcal subjects affected / exposed occurrences (all)	4 / 119 (3.36%) 4	5 / 121 (4.13%) 7	1 / 121 (0.83%) 1
Upper Respiratory Tract infection subjects affected / exposed occurrences (all)	5 / 119 (4.20%) 6	8 / 121 (6.61%) 9	11 / 121 (9.09%) 12
Metabolism and nutrition disorders Decreased Appetite subjects affected / exposed occurrences (all)	17 / 119 (14.29%) 21	22 / 121 (18.18%) 28	24 / 121 (19.83%) 40

<b>Non-serious adverse events</b>	PBO/ACWY		
Total subjects affected by non-serious adverse events subjects affected / exposed	86 / 108 (79.63%)		
Nervous system disorders Headache subjects affected / exposed occurrences (all)	32 / 108 (29.63%) 57		
General disorders and administration site conditions Chills subjects affected / exposed occurrences (all)	12 / 108 (11.11%) 17		
Fatigue subjects affected / exposed occurrences (all)	32 / 108 (29.63%) 55		
Injection Site Erythema subjects affected / exposed occurrences (all)	31 / 108 (28.70%) 40		
Injection Site Induration subjects affected / exposed occurrences (all)	24 / 108 (22.22%) 32		
Injection Site Pain subjects affected / exposed occurrences (all)	55 / 108 (50.93%) 74		
Pyrexia			

subjects affected / exposed occurrences (all)	7 / 108 (6.48%) 8		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	6 / 108 (5.56%)		
occurrences (all)	6		
Nausea			
subjects affected / exposed	9 / 108 (8.33%)		
occurrences (all)	12		
Respiratory, thoracic and mediastinal disorders			
Rhinitis Allergic			
subjects affected / exposed	7 / 108 (6.48%)		
occurrences (all)	8		
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	6 / 108 (5.56%)		
occurrences (all)	6		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	8 / 108 (7.41%)		
occurrences (all)	11		
Myalgia			
subjects affected / exposed	38 / 108 (35.19%)		
occurrences (all)	51		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	5 / 108 (4.63%)		
occurrences (all)	5		
Otitis Media Acute			
subjects affected / exposed	6 / 108 (5.56%)		
occurrences (all)	6		
Pharyngitis			
subjects affected / exposed	5 / 108 (4.63%)		
occurrences (all)	6		
Pharyngitis Stretococcal			

subjects affected / exposed	9 / 108 (8.33%)		
occurrences (all)	10		
Upper Respiratory Tract infection			
subjects affected / exposed	8 / 108 (7.41%)		
occurrences (all)	9		
Metabolism and nutrition disorders			
Decreased Appetite			
subjects affected / exposed	12 / 108 (11.11%)		
occurrences (all)	18		

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 May 2011	<ul style="list-style-type: none"><li>- replacement of study formulation MenABx2CWY (i.e., MenABCWY vaccine formulation containing a 'double' dose of rMenB, without OMV) with the MenABCWY+OMV formulation;</li><li>- addition of rMenB+OMV as a reference vaccine, thus adding a fourth study group and increasing the sample size from 360 to 480 subjects;</li><li>- addition of the third secondary objective (comparison with rMenB+OMV vaccine);</li><li>- broadening subjects' age range from 11 through 18 years to 10 through 25 years</li><li>- a Data Monitoring Committee (DMC) was formed</li></ul>
06 July 2012	<ul style="list-style-type: none"><li>- clarification that the purpose of the study was to select a MenABCWY formulation for further clinical development;</li><li>- secondary immunogenicity endpoints to include hSBA titers of <math>\geq 1:8</math> and 4-fold increase in hSBA titer for serogroup B strains</li></ul>
08 September 2012	<ul style="list-style-type: none"><li>- addition of desirability model as the second primary immunogenicity objective</li></ul>

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported