Clinical trial results:
A Phase 2b, Controlled, Observer-Blind, Multi-Center Study Assessing the Effectiveness, Immunogenicity and Safety of the 3rd Dose of GlaxoSmithKline Biologicals Meningococcal ABCWY Vaccine Administered to Healthy Adolescents in the U.S.

Summary

EudraCT number	2015-001030-16
Trial protocol	Outside EU/EEA
Global end of trial date	11 June 2015

Results information

Result version number	v3 (current)
This version publication date	07 September 2018
First version publication date	24 June 2016
Version creation reason	• New data added to full data set Endpoints for LLQ data are updated.

Trial information

Trial identification

Sponsor protocol code	205232

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02285777
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline Biologicals
Sponsor organisation address	Rue de l'Institut 89, Rixensart,, Belgium, B-1330
Public contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 44 2089904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 44 2089904466, GSKClinicalSupportHD@gsk.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	18 June 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 March 2015
Global end of trial reached?	Yes
Global end of trial date	11 June 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the effectiveness of the MenABCWY vaccine against a randomly selected panel of endemic US N. meningitidis serogroup B invasive disease strains as measured by bactericidal activity at 1:4 dilution using enc-hSBA at one month after the 3-dose series, when compared to a single dose of MenACWY.

Protection of trial subjects:

Standard immunization practices were observed and care was taken to administer the injection intramuscularly. As with all injectable vaccines, appropriate medical treatment and supervision was readily available in case of rare anaphylactic reactions following administration of the study vaccine. Epinephrine 1:1000 and diphenhydramine was available in case of any anaphylactic reactions. Care was taken to ensure that the vaccine is not injected into a blood vessel. The measures of safety used in this study are routine clinical procedures. They include a close vigilance for, and stringent reporting of, selected local and systemic adverse events routinely monitored in vaccine clinical studies as indicators of reactogenicity. The period of observation for AEs extends from the time the subject signs informed consent until he or she completes the final study visit (Visit Month 4) or terminates the study early (whichever comes first).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 December 2014
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: 189
Worldwide total number of subjects	189
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)	81

Adolescents (12-17 years)	97
Adults (18-64 years)	11
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

189 subjects were enrolled from 1 center in United States

Pre-assignment

Screening details:

An Interactive Response Technology (IRT) was used in the study. At Month 6 Visit of the parent study, IRT allocated the study vaccines (either MenABCWY or placebo) to the subject. Subject received either a 3rd dose of MenABCWY or one dose of a placebo, depending on their assigned vaccine group in parent study.

Period 1

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

Blinding implementation details:

Trial is observer-blinded. Observer-blind means that during the course of study, the subject, the parents/guardians of the subjects and the study personnel responsible for the evaluation of any study endpoint (e.g. safety and reactogenicity) will be unaware which vaccine was administered. The vaccine preparation and administration will be done by designated medical personnel who will not participate in any of the clinical study evaluations.

Arms

Are arms mutually exclusive?	Yes
Arm title	MenABCWY Group

Arm description:

Subjects who received 2 doses of MenABCWY vaccine in the parent study and a 3rd dose of MenABCWY vaccine in the current study.

Arm type	Experimental
Investigational medicinal product name	Meningococcal (groups A, C, W, and Y) oligosaccharide diphtheria CRM-197 conjugate combined with meningococcal (group B) multicomponent recombinant vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 dose of 0.5 millilitres

Arm title	MenACWY Group

Arm description:

Subjects who received 1 dose of placebo and 1 dose of MenACWY vaccine in the parent study and 1 dose of placebo in the current study.

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

Dosage and administration details:

1 dose of 0.5 millilitres

Number of subjects in period 1	MenABCWY Group	MenACWY Group
Started	95	94
Completed	90	91
Not completed	5	3
Consent withdrawn by subject	1	1
Lost to follow-up	4	2

Baseline characteristics

Reporting groups	
Reporting group title	MenABCWY Group
Reporting group description:	
Subjects who received 2 doses of MenABCWY vaccine in the parent study and a 3rd dose of MenABCWY vaccine in the current study.	
Reporting group title	MenACWY Group
Reporting group description:	
Subjects who received 1 dose of placebo and 1 dose of MenACWY vaccine in the parent study and 1 dose of placebo in the current study.	

Reporting group values	MenABCWY Group	MenACWY Group	Total
Number of subjects	95	94	189
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age <37 weeks)	0	0	0
Newborns (0-27 days)	0	0	0
Children (2-11 years)	36	45	81
Adolescents (12-17 years)	53	44	97
Adults (18-64 years)	6	5	11
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	12.8	12.4	
standard deviation	± 2.36	± 2.4	-
Gender categorical Units: Subjects			
Female	40	33	73
Male	55	61	116
Race/Ethnicity, Customized Units: Subjects			
AMERICAN INDIAN OR ALASKA NATIVE	0	2	2
ASIAN	1	0	1
BLACK OR AFRICAN AMERICAN	16	21	37
NATIVE HAWAIIAN OR OTHER PACIFIC ISLANDER	0	0	0
WHITE	74	66	140
OTHER	4	5	9

End points

End points reporting groups

Reporting group title	MenABCWY Group

Reporting group description:

Subjects who received 2 doses of MenABCWY vaccine in the parent study and a 3rd dose of MenABCWY vaccine in the current study.

Reporting group title	MenACWY Group

Reporting group description:

Subjects who received 1 dose of placebo and 1 dose of MenACWY vaccine in the parent study and 1 dose of placebo in the current study.

Primary: Percentages of subjects without bactericidal activity at 1:4 dilution against each US Neisseria meningitides (N. meningitidis) serogroup B strain at 1 month after the 3-dose vaccination series.

End point title	Percentages of subjects without bactericidal activity at 1:4 dilution against each US Neisseria meningitides (N. meningitidis) serogroup B strain at 1 month after the 3-dose vaccination series.

End point description:

The effectiveness of three doses of MenABCWY vaccine when compared to one dose of MenACWY vaccine against a panel of US N. meningitidis serogroup B invasive disease strains at 1 month after the 3-dose vaccination series was evaluated in terms of: the combined percentage of subjects without bactericidal activity at 1:4 dilution using the human Serum Bactericidal Assay (hSBA) against each strain in MenABCWY group and MenACWY group. The data provided is an average of the percentage of subjects without bactericidal activity at 1:4 dilution across all 110 strains.Analysis was performed on FAS-Effectiveness (Month 7)- included all screened subjects who provided informed consent & demographic &/or baseline screening assessments, received a subject ID & vaccination,& who provided evaluable serum sample with enc-hSBA result for at least 1 endemic N. meningitidis serogroup B invasive disease strain at Month 7.

End point type	Primary

End point timeframe:

At Month 7 (1 month after the 3-dose vaccination series)

End point values	MenABCWY Group	MenACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	93	93		
Units: Percentages of subjects				
number (not applicable)				
Month 7	21.1	73.7		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The Vaccine Effectiveness (VE) at 1 month after the 3-dose vaccination series for each strain is defined

as [1 - (percentage of subjects without bactericidal activity at 1:4 dilution in MenABCWY group/percentage of subjects without bactericidal activity at 1:4 dilution in MenACWY group)] x 100.The combined VE across all strains was computed by mean of a generalized linear model.

Comparison groups	MenABCWY Group v MenACWY Group
Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	= 0.0001
Method	Generalized Linear Model
Parameter estimate	Vaccine Effectiveness
Point estimate	71
Confidence interval	
level	95 %
sides	2-sided
lower limit	69
upper limit	73

Notes:

[1] - Pre-specified.

Secondary: Percentages of subjects without bactericidal activity at 1:4 dilution against each US N. meningitidis serogroup B strain at 4 months after the 3-dose vaccination series.

End point title	Percentages of subjects without bactericidal activity at 1:4 dilution against each US N. meningitidis serogroup B strain at 4 months after the 3-dose vaccination series.

End point description:

The effectiveness of three doses of MenABCWY vaccine when compared to one dose of MenACWY vaccine against a panel of US N. meningitidis serogroup B invasive disease strains at 4 months after the 3-dose vaccination series was evaluated in terms of: the combined percentage of subjects without bactericidal activity at 1:4 dilution using the hSBA against each strain in MenABCWY Group and MenACWY Group. The data provided is an average of the percentage of subjects without bactericidal activity at 1:4 dilution across all 110 strains.Analysis was performed on FAS-Effectiveness (Month 10)-included all screened subjects who provided informed consent & demographic &/or baseline screening assessments, received a subject ID & vaccination, & provided evaluable serum sample with the enc-hSBA result for at least 1 endemic N. meningitidis serogroup B invasive disease strain at Month 10

End point type	Secondary

End point timeframe:

At Month 10 (4 months after the 3-dose vaccination series)

End point values	MenABCWY Group	MenACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	90	90		
Units: Percentages of subjects				
number (not applicable)				
Month 10	33.9	69.9		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The Vaccine Effectiveness (VE) at 4 months after the 3-dose vaccination series for each strain is defined as [1 - (percentage of subjects without bactericidal activity at 1:4 dilution in MenABCWY group/percentage of subjects without bactericidal activity at 1:4 dilution in MenACWY group)] x 100. The combined VE across all strains was computed by mean of a generalized linear model.

Comparison groups	MenABCWY Group v MenACWY Group
Number of subjects included in analysis	180
Analysis specification	Pre-specified
Analysis type	other[2]
P-value	= 0.0001
Method	Generalized Linear Model
Parameter estimate	Vaccine Effectiveness
Point estimate	51
Confidence interval	
level	95 %
sides	2-sided
lower limit	48
upper limit	55

Notes:

[2] - Pre-specified.

Secondary: Percentages of subjects without bactericidal activity at 1:8 dilution against each US N. meningitidis serogroup B strain at 1 and 4 months after the 3-dose vaccination series.

End point title	Percentages of subjects without bactericidal activity at 1:8 dilution against each US N. meningitidis serogroup B strain at 1 and 4 months after the 3-dose vaccination series.

End point description:

The effectiveness of three doses of MenABCWY vaccine when compared to one dose of MenACWY vaccine against a panel of US N. meningitidis serogroup B invasive disease strains at 1 and 4 months after the 3-dose vaccination series were evaluated in terms of: the combined percentage of subjects without bactericidal activity at 1:8 dilution using the hSBA against each strain in MenABCWY Group and MenACWY Group. The data provided is an average of the percentage of subjects without bactericidal activity at 1:8 dilution across all 110 strains.Analysis was performed on FAS-Effectiveness (Months 7 & 10)- included all screened subjects who provided consent & demographic &/or baseline screening assessments, received subject ID & vaccination, & provided evaluable serum sample with the enc-hSBA result for at least 1 endemic N. meningitidis serogroup B invasive disease strain at Months 7 & 10.

End point type	Secondary

End point timeframe:

At Months 7 and 10 (1 and 4 months after the 3-dose vaccination series)

End point values	MenABCWY Group	MenACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	93	93		
Units: Percentages of subjects				
number (not applicable)				
Combined Serogroup B Strains (Month 7) (N-93, 93)	36.9	75.8		
Combined Serogroup B Strains (Month 10)(N-90,90)	60.3	79.6		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The Vaccine Effectiveness (VE) at 1 month after the 3-dose vaccination series for each strain is defined as [1 - (percentage of subjects without bactericidal activity at 1:8 dilution in MenABCWY group/percentage of subjects without bactericidal activity at 1:8 dilution in MenACWY group)] x 100. The combined VE across all strains was computed by mean of a generalized linear model.

Comparison groups	MenACWY Group v MenABCWY Group
Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	other[3]
P-value	= 0.0001
Method	Generalized Linear Model
Parameter estimate	Vaccine Effectiveness
Point estimate	51
Confidence interval	
level	95 %
sides	2-sided
lower limit	48
upper limit	54

Notes:

[3] - Pre-specified.

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

The Vaccine Effectiveness (VE) at 4 months after the 3-dose vaccination series for each strain is defined as [1 - (percentage of subjects without bactericidal activity at 1:8 dilution in MenABCWY group/percentage of subjects without bactericidal activity at 1:8 dilution in MenACWY group)] x 100. The combined VE across all strains was computed by mean of a generalized linear model.

Comparison groups	MenACWY Group v MenABCWY Group
Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	other[4]
P-value	= 0.0001
Method	Generalized Linear Model
Parameter estimate	Vaccine Effectiveness
Point estimate	24
Confidence interval	
level	95 %
sides	2-sided
lower limit	20
upper limit	28

Notes:

[4] - Pre-specified.

Secondary: Percentages of US N. meningitidis serogroup B strains killed at 1:4 and 1:8 dilutions at 1 and 4 months after the 3-dose vaccination series

End point title	Percentages of US N. meningitidis serogroup B strains killed at 1:4 and 1:8 dilutions at 1 and 4 months after the 3-dose vaccination series

End point description:

The mean percentage of US N. meningitidis serogroup B strains killed by each subject, at 1:4 and 1:8 dilutions before the 3-dose vaccination series, at Month 6 (PRE) and at 1 and 4 months after the 3-dose vaccination series (Month 7 and Month 10).Analysis was performed on FAS-Effectiveness (Months 6, 7 & 10)- included all screened subjects who provided consent & demographic &/or baseline screening assessments, got subject ID & vaccination, & provided serum sample with enc-hSBA result for at least 1 endemic N. meningitidis serogroup B invasive disease strain before Month 6 & at Months 7 & 10

End point type	Secondary

End point timeframe:

At Month 6 (before the 3-dose vaccination series) and at Months 7 and 10 (1 and 4 months after the 3-dose vaccination series)

End point values	MenABCWY Group	MenACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	93	93		
Units: Percentage				
arithmetic mean (standard deviation)				
1:4, PRE (N-93, 93)	56.97 (± 18.134)	22.94 (± 17.764)		
1:4, Month 7 (N-93, 93)	77.78 (± 10.041)	21.91 (± 16.885)		
1:4, Month 10 (N-93, 93)	62.37 (± 15.976)	22.49 (± 17.094)		
1:8, PRE (N-93, 93)	28.81 (± 17.086)	11.53 (± 11.705)		
1:8, Month 7 (N-93, 93)	56.95 (± 14.389)	11.4 (± 11.266)		
1:8, Month 10 (N-90, 90)	31.46 (± 19.434)	11.15 (± 10.774)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentages of subjects with enc-hSBA ≥ 1:4 and enc-hSBA ≥1:8 at 1 and 4 months after the 3-dose vaccination series

End point title	Percentages of subjects with enc-hSBA ≥ 1:4 and enc-hSBA ≥1:8 at 1 and 4 months after the 3-dose vaccination series

End point description:

The immunogenicity of three doses of MenABCWY vaccine compared to a single dose of MenACWY vaccine, in terms of percentages of subjects with enc-hSBA ≥ 1:4 and enc-hSBA ≥ 1:8 against four N. meningitidis serogroup B test strains (M14459, M07-0241084, 96217 and NZ98/254) at 1 and 4 months after the 3-dose vaccination series (Month 7 and Month 10).Analysis was performed on FAS-Immunogenicity (Months 7 &10)- included all screened subjects who provided consent & demographic &/or baseline screening assessments, received a subject ID & vaccination, & provided evaluable serum samples at Months 7 & 10 & whose immunogenicity assay result was available for at least one serogroup

B test strain.

End point type	Secondary

End point timeframe:

At Months 7 and 10 (1 and 4 months after the 3-dose vaccination series)

End point values	MenABCWY Group	MenACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	92	91		
Units: Percentages of subjects				
number (confidence interval 95%)				
M14459 (≥ 1:4, Month 7) (N-91, 90)	98 (92.3 to 99.73)	12 (6.3 to 20.8)		
M14459 (≥ 1:4, Month 10)(N-87, 90)	72 (61.8 to 81.5)	12 (6.3 to 20.8)		
M14459 (≥ 1:8, Month 7)(N-91, 90)	67 (56.4 to 76.5)	2 (0.27 to 7.8)		
M14459 (≥ 1:8, Month 10)(N-87, 90)	21 (12.7 to 30.7)	1 (0.03 to 6)		
M07-0241084 (≥ 1:4, Month 7)(N-90, 85)	81 (71.5 to 88.6)	21 (13.1 to 31.4)		
M07-0241084 (≥ 1:4, Month 10)(N-79, 78)	46 (34.3 to 57.2)	22 (13.2 to 32.6)		
M07-0241084 (≥ 1:8, Month 7)(N-90, 85)	38 (27.8 to 48.6)	5 (1.3 to 11.6)		
M07-0241084 (≥ 1:8, Month 10)(N-79, 78)	11 (5.3 to 20.5)	6 (2.1 to 14.3)		
96217 (≥ 1:4, Month 7)(N-89, 88)	99 (93.9 to 99.97)	48 (37 to 58.6)		
96217 (≥ 1:4, Month 10)(N-87,88)	100 (95.8 to 100)	41 (30.5 to 51.9)		
96217 (≥ 1:8, Month 7)(N-89, 88)	99 (93.9 to 99.97)	17 (9.9 to 26.6)		
96217 (≥ 1:8, Month 10)(N-87,88)	99 (93.8 to 99.97)	16 (9 to 25.2)		
NZ98/254 (≥ 1:4, Month 7)(N-84, 87)	76 (65.7 to 84.8)	1 (0.03 to 6.2)		
NZ98/254 (≥ 1:4, Month 10)(N-80, 83)	34 (23.6 to 45.2)	1 (0.03 to 6.5)		
NZ98/254 (≥ 1:8, Month 7)(N-84,87)	39 (28.8 to 50.5)	1 (0.03 to 6.2)		
NZ98/254 (≥ 1:8, Month 10)(N-80, 83)	4 (0.8 to 10.6)	0 (0 to 4.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: HT-hSBA Geometric Mean Titers (GMTs) against the N. meningitidis serogroup B test strains

End point title	HT-hSBA Geometric Mean Titers (GMTs) against the N. meningitidis serogroup B test strains

End point description:

The immunogenicity of three doses of MenABCWY vaccine compared to a single dose of MenACWY vaccine, in terms of HT-hSBA GMTs against four N. meningitidis serogroup B test strains (M14459, M07-0241084, 96217 and NZ98/254) after the 3-dose vaccination series.Analysis was performed on FAS-Immunogenicity (Months 7 &10)- included all screened subjects who provided consent & demographic &/or baseline screening assessments, received a subject ID & vaccination, & provided evaluable serum samples at Months 7 & 10 & whose immunogenicity assay result was available for at least one serogroup B test strain.

End point type	Secondary

End point timeframe:

At Months 7 and 10 (1 and 4 months after the 3-dose vaccination series)

End point values	MenABCWY Group	MenACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	91		
Units: Titers				
geometric mean (confidence interval 95%)				
M14459, Month 7(N-91,88)	23.12 (20 to 27)	1.1 (0.94 to 1.29)		
M14459, Month 10(N-88, 91)	3.93 (3.14 to 4.91)	1.18 (0.95 to 1.46)		
M07-0241084, Month 7(N-89,90)	12.26 (9.59 to 16)	1.74 (1.37 to 2.2)		
M07-0241084, Month 10(N-86, 90)	3.04 (2.36 to 3.92)	1.68 (1.31 to 2.14)		
96217, Month 7(N-90, 87)	367.29 (277 to 486)	4.02 (3.03 to 5.32)		
96217, Month 10(N-87, 85)	142.06 (105 to 191)	3.32 (2.46 to 4.48)		
NZ98/254, Month 7(N-89,89)	19.69 (16 to 24)	1.02 (0.85 to 1.23)		
NZ98/254, Month 10(N-87, 90)	3.75 (3.01 to 4.68)	1.04 (0.84 to 1.29)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentages of subjects with HT-hSBA titers against N. meningitidis serogroup B test strains ≥ Lower Limit of Quantitation (LLQ) at 1 month after the 3-dose vaccination series.

End point title	Percentages of subjects with HT-hSBA titers against N. meningitidis serogroup B test strains ≥ Lower Limit of Quantitation (LLQ) at 1 month after the 3-dose vaccination series.

End point description:

The immunogenicity of three doses of MenABCWY vaccine compared to a single dose of MenACWY, in terms of percentages of subjects with HT-hSBA titers ≥ LLQ against serogroup N. meningitidis B test strains (96217, M07-0241084,M14459 and NZ98/254), at 1 month after the 3-dose vaccination series.Analysis was performed on FAS-Immunogenicity (Month 7)- included all screened subjects who provided consent & demographic &/or baseline screening assessments, received a subject ID &

provided evaluable serum samples at Month 7 & whose immunogenicity assay result was available for at least one serogroup B test strain. The LLQ cut off values for strains 96217, M07-0241084,M14459 and NZ98/254 were 8.6, 8.9, 8 and 8.2 respectively.

End point type	Secondary

End point timeframe:

At Month 7 (1 month after the 3-dose vaccination series)

End point values	MenABCWY Group	MenACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	90		
Units: Percentages of subjects				
number (confidence interval 95%)				
96217(N-90, 87)	100 (96.0 to 100.0)	37 (26.7 to 47.8)		
M07-0241084(N-89, 90)	63 (52.0 to 72.9)	12 (6.3 to 20.8)		
M14459(N-91, 88)	90 (82.1 to 95.4)	1 (0.03 to 6.2)		
NZ98/254(N-89, 89)	79 (68.7 to 86.6)	1 (0.03 to 6.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentages of subjects with HT-hSBA titers against N. meningitidis serogroup B test strains ≥ LLQ at 4 months after the 3-dose vaccination series

End point title	Percentages of subjects with HT-hSBA titers against N. meningitidis serogroup B test strains ≥ LLQ at 4 months after the 3-dose vaccination series

End point description:

The immunogenicity of three doses of MenABCWY vaccine compared to a single dose of MenACWY, in terms of percentages of subjects with HT-hSBA titers ≥ LLQ against serogroup N. meningitidis B test strains (M14459, M07-0241084, 96217 and NZ98/254), at 4 months after the 3-dose vaccination series.Analysis was performed on FAS-Immunogenicity (Month 10)- included all screened subjects who provided informed consent & demographic &/or baseline screening assessments, received a subject ID & vaccination, & provided evaluable serum samples at Month 10 and whose immunogenicity assay result was available for at least one serogroup strain.The LLQ cut off values for the strains 96217, M07-0241084,M14459 and NZ98/254 were 8.6,8.9, 8 and 8.2 respectively.

End point type	Secondary

End point timeframe:

At Month 10 (4 months after the 3-dose vaccination series)

End point values	MenABCWY Group	MenACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	88	91		
Units: Percentages of subjects				
number (confidence interval 95%)				
96217(N-87, 85)	99 (93.8 to 99.97)	32 (22.1 to 42.8)		
M07-0241084(N-86,90)	23 (14.8 to 33.6)	12 (6.3 to 20.8)		
M14459(N-88,91)	36 (26.4 to 46.0)	3 (0.7 to 9.3)		
NZ98/254(N-87,90)	33 (23.6 to 44.3)	1 (0.03 to 6.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentages of subjects with a two-fold rise in HT-hSBA titers against the N. meningitidis serogroup B test strains at 1 and 4 months after the 3-dose vaccination series.

End point title	Percentages of subjects with a two-fold rise in HT-hSBA titers against the N. meningitidis serogroup B test strains at 1 and 4 months after the 3-dose vaccination series.

End point description:

The immunogenicity of three doses of MenABCWY vaccine compared to a single dose of MenACWY, in terms of the percentages of subjects with a two-fold rise in HT-hSBA titers against the N. meningitidis serogroup B test strains, at 1 and 4 months after the 3-dose vaccination series. The two-fold titers rise is defined as: a) for subjects with pre-vaccination (month 6 from the parent study) HT-hSBA titers < LLQ, postvaccination HT-hSBA titers ≥ 2 LLQ; b) for subjects with pre-vaccination (month 6 from the parent study) HT-hSBA titers ≥ LLQ, an increase of at least two times the pre-vaccination HT-hSBA titers.Analysis was performed on the FAS-Immunogenicity (months 7 and 10)- included all screened subjects who provided consent & demographic &/baseline screening assessments, received a subjects D & vaccination, & provided evaluable serum samples at months 7 & 10 & whose immunogenicity assay result was available for at least one serogroup B strain.

End point type	Secondary

End point timeframe:

At Months 7 and 10 (1 and 4 months after the 3-dose vaccination series)

End point values	MenABCWY Group	MenACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	90	90		
Units: Percentage of subjects				
number (confidence interval 95%)				
96217 (Month 7) (N-87,86)	87 (78.5 to 93.5)	12 (5.7 to 20.4)		
M07-0241084 (Month 7)(N-84,85)	38 (27.7 to 49.3)	1 (0.03 to 6.4)		
M14459 (Month 7)(N-90,87)	67 (56.0 to 76.3)	0 (0 to 4.1)		

NZ98/254 (Month 7)(N-88,88)	56 (44.7 to 66.3)	0 (0 to 4.1)		
96217 (Month 10)(N-84,84)	54 (42.4 to 64.5)	7 (2.7 to 14.9)		
M07-0241084 (Month 10)(N-81, 85)	0 (0 to 4.4)	4 (0.7 to 10.0)		
M14459 (Month 10)(N-87,90)	7 (2.6 to 14.4)	0 (0 to 4)		
NZ98/254 (Month 10)(N-86, 89)	13 (6.6 to 21.7)	0 (0 to 4.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentages of subjects with a three-fold rise in HT-hSBA titers against the N. meningitidis serogroup B test strains at 1 and 4 months after the 3-dose vaccination series.

End point title	Percentages of subjects with a three-fold rise in HT-hSBA titers against the N. meningitidis serogroup B test strains at 1 and 4 months after the 3-dose vaccination series.

End point description:

The immunogenicity of three doses of MenABCWY vaccine compared to a single dose of MenACWY, in terms of the percentages of subjects with a three-fold rise in HT-hSBA titers against the N. meningitidis serogroup B test strains, at 1 and 4 months after the 3-dose vaccination series. The three-fold titers rise is defined as: a) for subjects with pre-vaccination (month 6 from the parent study) HT-hSBA titers < LLQ, postvaccination HT-hSBA titers ≥ 2 LLQ; b) for subjects with pre-vaccination (month 6 from the parent study) HT-hSBA titers ≥ LLQ, an increase of at least three times the pre-vaccination HT-hSBA titers.Analysis was performed on the FAS-Immunogenicity (months 7 and 10)- included all screened subjects who provided consent & demographic &/baseline screening assessments, received a subjects D & vaccination, & provided evaluable serum samples at months 7 & 10 & whose immunogenicity assay result was available for at least one serogroup B strain.

End point type	Secondary

End point timeframe:

At months 7 and 10 (1 and 4 months after 3-dose vaccination series)

End point values	MenABCWY Group	MenACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	90	90		
Units: Percentage of subjects				
number (confidence interval 95%)				
96217 (Month 7)(N-87, 86)	79 (69.3 to 87.3)	5 (1.3 to 11.5)		
M07-0241084 (Month 7)(N-84, 85)	23 (14.2 to 33.1)	1 (0.03 to 6.4)		
M14459 (Month 7)(N-90,87)	41 (30.8 to 52.0)	0 (0 to 4.1)		
NZ98/254 (Month 7)(N-88,88)	41 (30.5 to 51.9)	0 (0 to 4.1)		
96217 (Month 10)(N-84, 84)	27 (18.2 to 38.2)	5 (1.3 to 11.8)		
M07-0241084 (Month 10)(N-81, 85)	0 (0 to 4.4)	2 (0.29 to 8.2)		
M14459 (Month 10)(N-87,90)	3 (0.7 to 9.8)	0 (0 to 4)		

NZ98/254 (Month 10)(N-86, 89)	5 (1.3 to 11.5)	0 (0 to 4.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentages of subjects with a four-fold rise in HT-hSBA titers against the N. meningitidis serogroup B test strains at 1 and 4 months after the 3-dose vaccination series.

End point title	Percentages of subjects with a four-fold rise in HT-hSBA titers against the N. meningitidis serogroup B test strains at 1 and 4 months after the 3-dose vaccination series.

End point description:

The immunogenicity of three doses of MenABCWY vaccine compared to a single dose of MenACWY, in terms of the percentages of subjects with a four-fold rise in HT-hSBA titers against the N. meningitidis serogroup B test strains, at 1 and 4 months after the 3-dose vaccination series. The four-fold titers rise is defined as: a) for subjects with pre-vaccination (month 6 from the parent study) HT-hSBA titers < LLQ, postvaccination HT-hSBA titers ≥ 4 LLQ; b) for subjects with pre-vaccination (month 6 from the parent study) HT-hSBA titers ≥ LLQ, an increase of at least four times the pre-vaccination HT-hSBA titers.Analysis was performed on the FAS-Immunogenicity (months 7 and 10)- included all screened subjects who provided consent & demographic &/baseline screening assessments, received a subjects D & vaccination, & provided evaluable serum samples at months 7 & 10 & whose immunogenicity assay result was available for at least one serogroup B strain.

End point type	Secondary

End point timeframe:

At Months 7 and 10 (1 and 4 months after the 3-dose vaccination series)

End point values	MenABCWY Group	MenACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	90	90		
Units: Percentages of subjects				
number (confidence interval 95%)				
96217 (Month 7)(N-87, 86)	63 (52.2 to 73.3)	3 (0.7 to 9.9)		
M07-0241084 (Month 7)(N-84, 85)	12 (5.9 to 20.8)	0 (0 to 4.2)		
M14459 (Month 7)(N-90, 87)	23 (15.1 to 33.4)	0 (0.0 to 4.1)		
NZ98/254 (Month 7)(N-88,88)	33 (23.3 to 43.8)	0 (0.0 to 4.1)		
96217 (Month 10)(N-84,84)	15 (8.5 to 25.0)	5 (1.3 to 11.8)		
M07-0241084 (Month 10)(N-81, 85)	0 (0 to 4.4)	1 (0.03 to 6.4)		
M14459 (Month 10)(N-87, 90)	3 (0.7 to 9.8)	0 (0 to 4)		
NZ98/254 (Month 10)(N-86,89)	2 (0.28 to 8.2)	0 (0 to 4.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: HT-hSBA GMTs against N. meningitidis serogroups A, C, W and Y.

End point title	HT-hSBA GMTs against N. meningitidis serogroups A, C, W and Y.

End point description:

The immunogenicity of three doses of MenABCWY compared to a single dose of MenACWY vaccine, in terms of HT-hSBA GMTs to serogroups A, C, W, and Y, at 1 and 4 months after the 3-dose vaccination series.Analysis was performed on the FAS-Immunogenicity (months 7 and 10)- included all screened subjects who provided consent & demographic &/baseline screening assessments, received a subjects D & vaccination, & provided evaluable serum samples at months 7 & 10 & whose immunogenicity assay result was available for at least one serogroup B strain.

End point type	Secondary

End point timeframe:

At Months 7 and 10 (1 and 4 months after the 3-dose vaccination series)

End point values	MenABCWY Group	MenACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	91		
Units: Titers				
geometric mean (confidence interval 95%)				
Men A, Month 7(N-91,87)	127.92 (91 to 179)	3.37 (2.41 to 4.73)		
Men A, Month 10(N-85,88)	36.5 (25 to 53)	2.73 (1.89 to 3.94)		
Men C, Month 7(N-85, 86)	521.64 (365 to 745)	18.34 (13 to 26)		
Men C, Month 10(N-86, 89)	291.19 (201 to 421)	15.4 (11 to 22)		
Men W, Month 7(N-83,88)	424.8 (310 to 581)	40.22 (30 to 54)		
Men W, Month 10(N-85,83)	147.4 (104 to 209)	23.01 (16 to 33)		
Men Y, Month 7(N-91,88)	204.84 (142 to 296)	13.27 (9.21 to 19)		
Men Y, Month 10(N-86,91)	83.42 (55 to 126)	11.85 (7.93 to 18)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentages of subjects with HT-hSBA titers against the N. meningitidis serogroup A, C, W and Y ≥ LLQ at 1 month after the 3- dose vaccination series

End point title	Percentages of subjects with HT-hSBA titers against the N. meningitidis serogroup A, C, W and Y ≥ LLQ at 1 month after the 3- dose vaccination series

End point description:

The immunogenicity of three doses of MenABCWY vaccine compared to a single dose of MenACWY, in terms of the percentages of subjects with HT-hSBA titers ≥ LLQ against serogroups A, C, W, Y, at 1 month after the 3-dose vaccination series.The LLQ cut off values for serogroups A,C,W and Y were 22.7,5.2, 39.6 and 14.7 respectively. Analysis was performed on FAS-Immunogenicity (Month 7)-included all screened subjects who provided consent & demographic &/or baseline screening assessments, received a subject ID & vaccination, & provided evaluable serum samples at Month 7 & whose immunogenicity assay result was available for at least one serogroup A, C, W and Y test strain.

End point type	Secondary

End point timeframe:

At Month 7 (1 month after the 3-dose vaccination series)

End point values	MenABCWY Group	MenACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	88		
Units: Percentages of subjects				
number (confidence interval 95%)				
Men A(N-91, 87)	98 (92.3 to 99.73)	24 (15.6 to 34.5)		
Men C(N-85,86)	100 (95.8 to 100.0)	73 (62.6 to 82.2)		
Men W(N-83,88)	99 (93.5 to 99.97)	60 (49.2 to 70.5)		
Men Y(N-91,88)	100 (96.0 to 100)	57 (45.8 to 67.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentages of subjects with HT-hSBA titers against the N. meningitidis serogroup A, C, W and Y ≥ LLQ at 4 months after the 3-dose vaccination series

End point title	Percentages of subjects with HT-hSBA titers against the N. meningitidis serogroup A, C, W and Y ≥ LLQ at 4 months after the 3-dose vaccination series

End point description:

The immunogenicity of three doses of MenABCWY vaccine compared to a single dose of MenACWY, in terms of the percentages of subjects with HT-hSBA titers ≥ LLQ against serogroups A, C, W, Y, at 4 months after the 3-dose vaccination series.The LLQ cut off values for serogroups A, C, W and Y were 22.7,5.2,39.6 and 14.7 respectively.Analysis was performed on FAS-Immunogenicity (Month 10)-included all screened subjects who provided informed consent & demographic &/or baseline screening assessments, received a subject ID & vaccination, & provided evaluable serum samples at Month 10 and whose immunogenicity assay result was available for at least one serogroup B strain

End point type	Secondary

End point timeframe:

At Month 10 (4 months after the 3-dose vaccination series)

End point values	MenABCWY Group	MenACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	86	91		
Units: Percentages of subjects				
number (confidence interval 95%)				
Men A(N-85,88)	81 (71.2 to 88.8)	18 (10.8 to 27.8)		
Men C(N-86,89)	100 (95.8 to 100.0)	69 (57.8 to 78.0)		
Men W(N-85,83)	89 (80.9 to 95.0)	51 (39.4 to 61.8)		
Men Y(N-86,91)	86 (76.9 to 92.6)	53 (42.0 to 63.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with two-fold rise in HT-hSBA titers against the N. meningitidis serogroups A, C,W and Y at 1 and 4 months after the 3-dose vaccination series.

End point title	Percentage of subjects with two-fold rise in HT-hSBA titers against the N. meningitidis serogroups A, C,W and Y at 1 and 4 months after the 3-dose vaccination series.

End point description:

The immunogenicity of three doses of MenABCWY vaccine compared to a single dose of MenACWY, in terms of the percentages of subjects with a two-fold rise in HT-hSBA titers against the N. meningitidis serogroups A, C, W and Y at 1 and 4 months after the 3-dose vaccination series. The two-fold titers rise is defined as: a) for subjects with pre-vaccination(month 6 from the parent study) HT-hSBA titers < LLQ, postvaccination HT-hSBA titers ≥ 2 LLQ; b) for subjects with pre-vaccination(month 6 from the parent study) HT-hSBA titers ≥ LLQ, an increase of at least two times the pre-vaccination HT-hSBA titers.Analysis was performed on the FAS-Immunogenicity (months 7 and 10)- included all screened subjects who provided consent & demographic &/baseline screening assessments, received a subject ID & vaccination, & provided evaluable serum samples at months 7 & 10 & whose immunogenicity assay result was available for at least one serogroup B strain.

End point type	Secondary

End point timeframe:

At Months 7 and 10 (1 and 4 months after the 3-dose vaccination series)

End point values	MenABCWY Group	MenACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	88		
Units: Percentage of subjects				
number (confidence interval 95%)				
Men A, Month 7(N-83,85)	88 (79.0 to 94.1)	2 (0.29 to 8.2)		
Men C, Month 7(N-84,84)	87 (77.8 to 93.3)	2 (0.29 to 8.3)		
Men W, Month 7(N-81, 84)	83 (72.7 to 90.2)	5 (1.3 to 11.8)		
Men Y, Month 7(N-89, 85)	57 (46.4 to 67.7)	2 (0.29 to 8.2)		
Men A, Month 10(N-77, 86)	32 (22.2 to 44.1)	1 (0.03 to 6.3)		
Men C, Month 10(N-85, 87)	56 (45.3 to 67.2)	8 (3.3 to 15.9)		
Men W, Month 10(N-83,79)	24 (15.4 to 34.7)	1 (0.03 to 6.9)		
Men Y, Month 10(N-84, 88)	26 (17.2 to 36.9)	3 (0.7 to 9.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with three-fold rise in HT-hSBA titers against the N. meningitidis serogroups A, C, W and Y at 1 and 4 months after the 3-dose vaccination series.

End point title	Percentage of subjects with three-fold rise in HT-hSBA titers against the N. meningitidis serogroups A, C, W and Y at 1 and 4 months after the 3-dose vaccination series.

End point description:

The immunogenicity of three doses of MenABCWY vaccine compared to a single dose of MenACWY, in terms of the percentages of subjects with a three-fold rise in HT-hSBA titers against the N. meningitidis serogroups A, C, W and Y, at 1 and 4 months after the 3-dose vaccination series. The three-fold titers rise is defined as: a) for subjects with pre-vaccination(month 6 from the parent study) HT-hSBA titers < LLQ, postvaccination HT-hSBA titers ≥ 3 LLQ; b) for subjects with pre-vaccination(month 6 from the parent study) HT-hSBA titers ≥ LLQ, an increase of at least three times the pre-vaccination HT-hSBA titers.Analysis was performed on the FAS-Immunogenicity (months 7 and 10)- included all screened subjects who provided consent & demographic &/baseline screening assessments, received a subject ID & vaccination, & provided evaluable serum samples at months 7 & 10 & whose immunogenicity assay result was available for at least one serogroup B strain.

End point type	Secondary

End point timeframe:

At Months 7 and 10 (1 and 4 months after the 3-dose vaccination series)

End point values	MenABCWY Group	MenACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	88		
Units: Percentage of subjects				
number (confidence interval 95%)				
Men A, Month 7(N-83,85)	69 (57.6 to 78.4)	0 (0 to 4.2)		
Men C, Month 7(N-84, 84)	60 (48.3 to 70.1)	1 (0.03 to 6.5)		
Men W, Month 7(N-81, 84)	67 (55.3 to 76.8)	0 (0 to 4.3)		
Men Y, Month 7(N-89, 85)	39 (29.1 to 50.3)	0 (0 to 4.2)		
Men A, Month 10(N-77,86)	16 (8.3 to 25.6)	1 (0.03 to 6.3)		
Men C, Month 10(N-85,87)	29 (20.0 to 40.3)	5 (1.3 to 11.4)		
Men W, Month 10(N-83, 79)	13 (6.8 to 22.5)	0 (0 to 4.6)		
Men Y, Month 10(N-84,88)	15 (8.5 to 25.0)	2 (0.28 to 8.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with four-fold rise in HT-hSBA titers against the N. meningitidis serogroups A, C, W and Y at 1 and 4 months after the 3-dose vaccination series.

End point title	Percentage of subjects with four-fold rise in HT-hSBA titers against the N. meningitidis serogroups A, C, W and Y at 1 and 4 months after the 3-dose vaccination series.

End point description:

The immunogenicity of three doses of MenABCWY vaccine compared to a single dose of MenACWY, in terms of the percentages of subjects with a four-fold rise in HT-hSBA titers against the N. meningitidis serogroups A, C, W and Y, at 1 and 4 months after the 3-dose vaccination series. The four-fold titers rise is defined as: a) for subjects with pre-vaccination(month 6 from the parent study) HT-hSBA titers < LLQ, postvaccination HT-hSBA titers ≥ 4 LLQ; b) for subjects with pre-vaccination(month 6 from the parent study) HT-hSBA titers ≥ LLQ, an increase of at least four times the pre-vaccination HT-hSBA titers.Analysis was performed on the FAS-Immunogenicity (months 7 and 10)- included all screened subjects who provided consent & demographic &/baseline screening assessments, received a subject ID & vaccination, & provided evaluable serum samples at months 7 & 10 & whose immunogenicity assay result was available for at least one serogroup B strain.

End point type	Secondary

End point timeframe:

At Months 7 and 10 (1 and 4 months after the 3-dose vaccination series)

End point values	MenABCWY Group	MenACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	88		
Units: Percentage of subjects				
number (confidence interval 95%)				
Men A, Month 7(N-83,85)	53 (41.7 to 64.1)	0 (0 to 4.2)		
Men C, Month 7(N-84,84)	49 (37.7 to 60.0)	1 (0.03 to 6.5)		
Men W, Month 7(N-81, 84)	49 (38.1 to 60.7)	0 (0 to 4.3)		
Men Y, Month 7(N-89, 85)	28 (19.1 to 38.6)	0 (0 to 4.2)		
Men A, Month 10(N-77, 86)	6 (2.1 to 14.5)	1 (0.03 to 6.3)		
Men C, Month 10(N-85, 87)	21 (13.1 to 31.4)	2 (0.28 to 8.1)		
Men W, Month 10(N-83,79)	8 (3.5 to 16.6)	0 (0 to 4.6)		
Men Y, Month 10(N-84, 88)	6 (2.0 to 13.4)	1 (0.03 to 6.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentages of Subjects With HT-hSBA Titers Against N. Meningitidis Serogroup B Test Strains ≥ 5, ≥ 8, ≥ 16, ≥ 32, ≥ 64, ≥ 128 at 1 Month After the 3-dose Vaccination Series

End point title	Percentages of Subjects With HT-hSBA Titers Against N. Meningitidis Serogroup B Test Strains ≥ 5, ≥ 8, ≥ 16, ≥ 32, ≥ 64, ≥ 128 at 1 Month After the 3-dose Vaccination Series

End point description:

The immunogenicity of three doses of MenABCWY vaccine compared to a single dose of MenACWY, in terms of percentages of subjects with HT-hSBA titers ≥ 5, ≥ 8, ≥ 16, ≥ 32, ≥ 64, ≥ 128 against serogroup N. meningitidis B test strains (M14459, M07-0241084, 96217 and NZ98/254), at 1 month after the 3-dose vaccination series.Analysis was performed on FAS-Immunogenicity (Month 7)- included all screened subjects who provided consent & demographic &/or baseline screening assessments, received a subject ID & vaccination, & provided evaluable serum samples at Month 7 & whose immunogenicity assay result was available for at least one serogroup B test strain.

End point type	Secondary

End point timeframe:

At Month 7 (1 month after the 3-dose vaccination series)

End point values	MenABCWY Group	MenACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	90		
Units: Percentage of subjects				
number (confidence interval 95%)				
96217, ≥ 5 (N-90, 87)	100 (96 to 100)	38 (27.7 to 49)		

96217, ≥ 8 (N-90, 87)	100 (96 to 100)	37 (26.7 to 47.8)		
96217, ≥ 16 (N-90, 87)	100 (96 to 100)	25 (16.6 to 35.7)		
96217, ≥ 32 (N-90, 87)	100 (96 to 100)	15 (8.2 to 24.2)		
96217, ≥ 64 (N-90, 87)	99 (94 to 99.97)	8 (3.3 to 15.9)		
96217, ≥ 128 (N-90, 87)	93 (86.1 to 97.5)	3 (0.7 to 9.7)		
M07-0241084, ≥ 5 (N-89,90)	82 (72.5 to 89.4)	16 (8.8 to 24.7)		
M07-0241084, ≥ 8(N-89,90)	67 (56.7 to 77)	12 (6.3 to 20.8)		
M07-0241084, ≥ 16(N-89,90)	46 (35.4 to 57)	8 (3.2 to 15.4)		
M07-0241084, ≥ 32(N-89,90)	20 (12.4 to 30.1)	3 (0.7 to 9.4)		
M07-0241084, ≥ 64(N-89,90)	6 (1.8 to 12.6)	2 (0.27 to 7.8)		
M07-0241084, ≥ 128(N-89,90)	0 (0 to 4.1)	0 (0 to 4)		
M14459, ≥ 5 (N-91,88)	95 (87.6 to 98.2)	1 (0.03 to 6.2)		
M14459, ≥ 8(N-91,88)	90 (82.1 to 95.4)	1 (0.03 to 6.2)		
M14459, ≥ 16(N-91,88)	71 (61 to 80.4)	1 (0.03 to 6.2)		
M14459, ≥ 32(N-91,88)	34 (24.5 to 44.7)	1 (0.03 to 6.2)		
M14459, ≥ 64(N-91,88)	11 (5.4 to 19.3)	0 (0 to 4.1)		
M14459, ≥ 128(N-91,88)	3 (0.7 to 9.3)	0 (0 to 4.1)		
NZ98/254, ≥ 5 (N-89,89)	89 (80.3 to 94.5)	1 (0.03 to 6.1)		
NZ98/254, ≥ 8(N-89,89)	79 (68.7 to 86.6)	1 (0.03 to 6.1)		
NZ98/254, ≥ 16(N-89,89)	61 (49.7 to 70.9)	0 (0 to 4.1)		
NZ98/254, ≥ 32(N-89,89)	37 (27.1 to 48)	0 (0 to 4.1)		
NZ98/254, ≥ 64(N-89,89)	10 (4.7 to 18.3)	0 (0 to 4.1)		
NZ98/254, ≥ 128(N-89,89)	4 (1.2 to 11.1)	0 (0 to 4.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentages of Subjects With HT-hSBA Titers Against N. Meningitidis Serogroup B Test Strains ≥ 5, ≥ 8, ≥ 16, ≥ 32, ≥ 64, ≥ 128 at 4 Months After the 3-dose Vaccination Series

End point title	Percentages of Subjects With HT-hSBA Titers Against N. Meningitidis Serogroup B Test Strains ≥ 5, ≥ 8, ≥ 16, ≥ 32, ≥ 64, ≥ 128 at 4 Months After the 3-dose Vaccination Series

End point description:

The immunogenicity of three doses of MenABCWY vaccine compared to a single dose of MenACWY, in terms of percentages of subjects with HT-hSBA titers ≥ 5, ≥ 8, ≥ 16, ≥ 32, ≥ 64, ≥ 128 against serogroup N. meningitidis B test strains (M14459, M07-0241084, 96217 and NZ98/254), at 4 months after the 3-dose vaccination series.Analysis was performed on FAS-Immunogenicity (Month 10)-included all screened subjects who provided consent & demographic &/or baseline screening assessments, received a subject ID & vaccination, & provided evaluable serum samples at Month 10 &

whose immunogenicity assay result was available for at least one serogroup B test strain.

End point type	Secondary

End point timeframe:

At Month 10 (4 months after the 3-dose vaccination series)

End point values	MenABCWY Group	MenACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	88	91		
Units: Percentage of subjects				
number (confidence interval 95%)				
96217, ≥ 5 (N-87, 85)	99 (93.8 to 99.97)	35 (25.2 to 46.4)		
96217, ≥ 8(N-87, 85)	99 (93.8 to 99.97)	33 (23.1 to 44)		
96217, ≥ 16(N-87, 85)	98 (91.9 to 99.72)	21 (13.1 to 31.4)		
96217, ≥ 32(N-87, 85)	94 (87.1 to 98.1)	16 (9.3 to 26.1)		
96217, ≥64(N-87, 85)	85 (75.8 to 91.8)	6 (1.9 to 13.2)		
96217, ≥ 128(N-87, 85)	56 (45.3 to 66.9)	2 (0.29 to 8.2)		
M07-0241084, ≥ 5 (N-86, 90)	38 (28.1 to 49.5)	17 (9.6 to 26)		
M07-0241084, ≥ 8 (N-86, 90)	24 (15.8 to 34.9)	12 (6.3 to 20.8)		
M07-0241084, ≥ 16 (N-86, 90)	9 (4.1 to 17.5)	9 (3.9 to 16.8)		
M07-0241084, ≥ 32 (N-86, 90)	1 (0.03 to 6.3)	3 (0.7 to 9.4)		
M07-0241084, ≥ 64 (N-86, 90)	1 (0.03 to 6.3)	2 (0.27 to 7.8)		
M07-0241084, ≥ 128 (N-86, 90)	0 (0 to 4.2)	1 (0.03 to 6)		
M14459, ≥ 5(N-88, 91)	49 (38.1 to 59.8)	4 (1.2 to 10.9)		
M14459, ≥ 8(N-88, 91)	36 (26.4 to 47.3)	3 (0.7 to 9.3)		
M14459, ≥ 16(N-88, 91)	17 (9.9 to 26.6)	1 (0.03 to 6)		
M14459, ≥ 32(N-88, 91)	6 (1.9 to 12.8)	0 (0 to 4)		
M14459, ≥ 64(N-88, 91)	1 (0.03 to 6.2)	0 (0 to 4)		
M14459, ≥ 128(N-88, 91)	0 (0 to 4.1)	0 (0 to 4)		
NZ98/254, ≥ 5 (N-87, 90)	44 (33.1 to 54.7)	1 (0.03 to 6)		
NZ98/254, ≥ 8 (N-87, 90)	34 (24.6 to 45.4)	1 (0.03 to 6)		
NZ98/254, ≥ 16 (N-87, 90)	16 (9.1 to 25.5)	0 (0 to 4)		
NZ98/254, ≥ 32 (N-87, 90)	5 (1.3 to 11.4)	0 (0 to 4)		
NZ98/254, ≥ 64 (N-87, 90)	2 (0.28 to 8.1)	0 (0 to 4)		
NZ98/254, ≥ 128 (N-87, 90)	2 (0.28 to 8.1)	0 (0 to 4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentages of Subjects With HT-hSBA Titers Against the N. Meningitidis Serogroup A, C, W and Y ≥ 8, ≥ 16, ≥ 32, ≥ 64, ≥128 at 1 Month After the 3- Dose Vaccination Series

End point title	Percentages of Subjects With HT-hSBA Titers Against the N. Meningitidis Serogroup A, C, W and Y ≥ 8, ≥ 16, ≥ 32, ≥ 64, ≥128 at 1 Month After the 3- Dose Vaccination Series

End point description:

The immunogenicity of three doses of MenABCWY vaccine compared to a single dose of MenACWY, in terms of the percentages of subjects with HT-hSBA titers ≥ 8, ≥ 16, ≥ 32, ≥ 64, ≥128 against serogroups A, C, W, Y, at 1 month after the 3-dose vaccination series.Analysis was performed on FAS-Immunogenicity (Month 7)- included all screened subjects who provided consent & demographic &/or baseline screening assessments, received a subject ID & vaccination, & provided evaluable serum samples at Month 7 & whose immunogenicity assay result was available for at least one serogroup A, C, W and Y test strain.

End point type	Secondary

End point timeframe:

At Month 7 (1 month after the 3-dose vaccination series)

End point values	MenABCWY Group	MenACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	88		
Units: Percentage of subjects				
number (confidence interval 95%)				
Men A, ≥ 8 (N-91, 87)	98 (92.3 to 99.73)	30 (20.5 to 40.6)		
Men A, ≥ 16(N-91, 87)	98 (92.3 to 99.73)	26 (17.6 to 37)		
Men A, ≥ 32(N-91, 87)	98 (92.3 to 99.73)	22 (13.7 to 32)		
Men A, ≥ 64(N-91, 88)	86 (76.8 to 92.2)	13 (6.5 to 21.5)		
Men A, ≥ 128(N-91, 87)	56 (45.2 to 66.4)	8 (3.3 to 15.9)		
Men C, ≥ 8(N-85, 86)	100 (95.8 to 100)	71 (60.1 to 80.2)		
Men C, ≥ 16(N-85, 86)	99 (93.6 to 99.97)	51 (40.1 to 62.1)		
Men C, ≥ 32(N-85, 86)	99 (93.6 to 99.97)	33 (22.8 to 43.5)		
Men C, ≥ 64(N-85, 86)	99 (93.6 to 99.97)	26 (16.8 to 36.1)		
Men C, ≥ 128(N-85, 86)	91 (82.3 to 95.8)	19 (11 to 28.4)		
Men W, ≥ 8(N-83, 88)	100 (95.7 to 100)	86 (77.4 to 92.8)		
Men W, ≥ 16(N-83, 88)	100 (95.7 to 100)	77 (67.1 to 85.5)		
Men W, ≥ 32(N-83, 88)	99 (93.5 to 99.97)	61 (50.4 to 71.6)		
Men W, ≥ 64(N-83, 88)	99 (93.5 to 99.97)	45 (34.8 to 56.4)		

Men W, ≥ 128(N-83, 88)	89 (80.4 to 94.9)	24 (15.4 to 34.1)		
Men Y, ≥ 8(N-91, 88)	100 (96 to 100)	61 (50.4 to 71.6)		
Men Y, ≥ 16(N-91, 88)	100 (96 to 100)	56 (44.7 to 66.3)		
Men Y, ≥ 32(N-91, 88)	95 (87.6 to 98.2)	44 (33.7 to 55.3)		
Men Y, ≥ 64(N-91, 88)	81 (71.8 to 88.7)	27 (18.3 to 37.8)		
Men Y, ≥ 128(N-91, 88)	65 (54.1 to 74.6)	14 (7.2 to 22.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentages of Subjects With HT-hSBA Titers Against the N. Meningitidis Serogroup A, C, W and Y ≥ 8, ≥ 16, ≥ 32, ≥ 64, ≥128 at 4 Months After the 3-dose Vaccination Series

End point title	Percentages of Subjects With HT-hSBA Titers Against the N. Meningitidis Serogroup A, C, W and Y ≥ 8, ≥ 16, ≥ 32, ≥ 64, ≥128 at 4 Months After the 3-dose Vaccination Series

End point description:

The immunogenicity of three doses of MenABCWY vaccine compared to a single dose of MenACWY, in terms of the percentages of subjects with HT-hSBA titers≥ 8, ≥ 16, ≥ 32, ≥ 64, ≥ 128 against serogroups A, C, W, Y, at 4 months after the 3-dose vaccination series.Analysis was performed on FAS-Immunogenicity (Month 10)- included all screened subjects who provided consent & demographic &/or baseline screening assessments, received a subject ID & vaccination, & provided evaluable serum samples at Month 10 & whose immunogenicity assay result was available for at least one serogroup A, C, W and Y test strain.

End point type	Secondary

End point timeframe:

At Month 10 (4 months after the 3-dose vaccination series)

End point values	MenABCWY Group	MenACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	86	91		
Units: Percentage of subjects				
number (confidence interval 95%)				
Men A, ≥ 8 (N-85,88)	86 (76.6 to 92.5)	25 (16.4 to 35.4)		
Men A, ≥ 16(N-85,88)	84 (73.9 to 90.7)	23 (14.5 to 32.9)		
Men A, ≥ 32(N-85,88)	72 (61 to 81)	18 (10.8 to 27.8)		
Men A, ≥ 64(N-85,88)	46 (35 to 57)	8 (3.3 to 15.7)		
Men A, ≥ 128(N-85,88)	14 (7.5 to 23.4)	7 (2.5 to 14.3)		

Men C, ≥ 8(N-86,89)	100 (95.8 to 100)	65 (54.3 to 75)		
Men C, ≥ 16(N-86,89)	98 (91.9 to 99.72)	48 (37.6 to 59.2)		
Men C, ≥ 32(N-86,89)	97 (90.1 to 99.3)	34 (24 to 44.5)		
Men C, ≥ 64(N-86,91)	86 (76.9 to 92.6)	26 (17.1 to 36.2)		
Men C, ≥ 128(N-86,91)	74 (63.9 to 83.2)	16 (8.9 to 25)		
Men W, ≥ 8(N-85,83)	99 (93.6 to 99.97)	75 (64 to 83.6)		
Men W, ≥ 16(N-85,83)	98 (91.8 to 99.71)	66 (55.1 to 76.3)		
Men W, ≥ 32(N-85,83)	94 (86.8 to 98.1)	58 (46.5 to 68.6)		
Men W, ≥ 64(N-85,83)	75 (64.7 to 84)	36 (25.9 to 47.4)		
Men W, ≥ 128(N-85,83)	52 (40.7 to 62.7)	18 (10.5 to 28)		
Men Y, ≥ 8(N-86,91)	91 (82.5 to 95.9)	58 (47.4 to 68.5)		
Men Y, ≥ 16(N-86,91)	86 (76.9 to 92.6)	51 (39.9 to 61.2)		
Men Y, ≥ 32(N-86,91)	77 (66.4 to 85.2)	38 (28.4 to 49.2)		
Men Y, ≥ 64(N-86,91)	62 (50.5 to 71.9)	20 (12.2 to 29.4)		
Men Y, ≥ 128(N-86,91)	40 (29.2 to 50.7)	9 (3.9 to 16.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any solicited local or systemic Adverse Events (AEs)

End point title	Number of subjects reporting any solicited local or systemic Adverse Events (AEs)

End point description:

Number of subjects reporting any solicited local or systemic AEs from Day 1 (6 hours) to Day 7 after any meningococcal vaccination is reported. Assessed solicited local symptoms were induration, erythema and pain. Assessed solicited general symptoms were fatigue, myalgia, arthralgia, headache, fever, chills and loss of appetite. Other solicited data included prevention of pain/fever and treatment of pain/fever. Any = occurrence of the symptom regardless of intensity grade.Analysis was performed on Safety Set (solicited AEs & other solicited reactions)-included all screened subjects who provided consent & demographic &/or baseline screening assessments, received a subject ID & a study vaccination, & provided post-vaccination reactogenicity data.

End point type	Secondary

End point timeframe:

Day 1 (6 hours) to Day 7 after vaccination

End point values	MenABCWY Group	MenACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	90	87		
Units: Participants				
Any (Vacc.1, N=90,87)	62	25		
Any Local Reactions(Vacc.1, N=90,87)	60	15		
Any Systemic Reactions(Vacc.1, N=90,87)	27	15		
Induration (mm)(Vacc.1, N=88,87)	6	0		
Erythema (mm)(Vacc.1, N=87,86)	6	0		
Pain(Vacc.1, N=88,87)	59	15		
Nausea(Vacc.1, N=87,87)	5	5		
Fatigue(Vacc.1, N=87,87)	14	11		
Myalgia(Vacc.1, N=87,85)	13	3		
Arthralgia (Vacc.1, N=86,85)	9	0		
Headache(Vacc.1, N=88,87)	13	9		
Fever(Vacc.1, N=90,85)	0	1		
Chills(Vacc.1, N=88,87)	2	3		
Loss of appetite(Vacc.1, N=88,87)	3	3		
Prevention of pain/fever (Vacc.1, N=85,84)	0	0		
Treatment of pain/fever(Vacc.1, N=85,84)	12	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any unsolicited AEs

End point title	Number of subjects reporting any unsolicited AEs

End point description:

The number of subjects reporting unsolicited AEs after any vaccination is reported. An unsolicited AE covers any untoward medical occurrence in a clinical investigation subject temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product and reported in addition to those solicited during the clinical study and any solicited symptom with onset outside the specified period of follow-up for solicited symptoms. Any was defined as the occurrence of any unsolicited AE regardless of intensity grade or relation to vaccination.Analysis was performed on Safety set (unsolicited AEs)- included all screened subjects who provided informed consent & demographic and/or baseline screening assessments, received a subject ID and a study vaccination, and had post-vaccination unsolicited adverse event records.

End point type	Secondary

End point timeframe:

Day 1 to Day 30 after any vaccination

End point values	MenABCWY Group	MenACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	93	93		
Units: Participants				
Participants	14	11		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any serious adverse events (SAEs), medically-attended AEs and AEs leading to premature withdrawal.

End point title	Number of subjects reporting any serious adverse events (SAEs), medically-attended AEs and AEs leading to premature withdrawal.

End point description:

The number of subjects reporting any SAEs, medically-attended AEs and AEs leading to premature withdrawal during the entire study period is reported. SAEs assessed include medical occurrences that result in death, are life-threatening, require hospitalization or prolongation of hospitalization or result in disability/incapacity. MAEs were defined as events for which the subject received medical attention defined as hospitalization, an emergency room visit, or a visit to or from medical personnel (medical doctor) for any reason. Any was defined as the occurrence of any unsolicited AE regardless of intensitygrade or relation to vaccination.Analysis was performed on Safety Set (overall)- included all screened subjects who provide informed consent and demographic and/or baseline screening assessments, received a subject ID and a study vaccination, and have either post-vaccination reactogenicity data or post-vaccination unsolicited adverse event records.

End point type	Secondary

End point timeframe:

During the entire study period (from Day 0 up to Month 10)

End point values	MenABCWY Group	MenACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	95	94		
Units: Participants				
Any SAEs(N=93,93)	0	0		
Any Medically Attended AEs(N=93,93)	14	20		
Any AEs leading to premature withdrawal(N=95,94)	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited local and general AEs were collected from Day 1 to Day 7. Unsolicited AEs were collected from Day 1 to Day 30. SAEs, medically-attended AEs and AEs leading to withdrawal are collected for the entire duration of the study (from Day 0 to Month 10)

Adverse event reporting additional description:

Total number of subjects at risk for the frequent AEs were analysed from the exposed set & the number of subjects at risk for each of the individual adverse event were analysed from overall safety set. Therefore, the number of subjects at risk for each adverse event is lesser than total number of subjects at risk

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups

Reporting group title	MenACWY Group

Reporting group description:

Subjects who received 1 dose of placebo and 1 dose of MenACWY vaccine in the parent study and 1 dose of placebo in the current study.

Reporting group title	MenABCWY Group

Reporting group description:

Subjects who received 2 doses of MenABCWY vaccine in the parent study and a 3rd dose of MenABCWY vaccine in the current study.

Serious adverse events	MenACWY Group	MenABCWY Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 94 (0.00%)	0 / 95 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

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

Non-serious adverse events	MenACWY Group	MenABCWY Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	27 / 94 (28.72%)	63 / 95 (66.32%)	
Nervous system disorders			
Headache			
subjects affected / exposed[1]	9 / 93 (9.68%)	14 / 93 (15.05%)	
occurrences (all)	27	25	
General disorders and administration site conditions			

Fatigue			
subjects affected / exposed[2]	11 / 93 (11.83%)	14 / 93 (15.05%)	
occurrences (all)	24	32	
Injection site erythema			
subjects affected / exposed[3]	4 / 93 (4.30%)	16 / 93 (17.20%)	
occurrences (all)	12	44	
Injection site induration			
subjects affected / exposed[4]	3 / 93 (3.23%)	16 / 93 (17.20%)	
occurrences (all)	10	57	
Injection site pain			
subjects affected / exposed[5]	15 / 93 (16.13%)	60 / 93 (64.52%)	
occurrences (all)	23	155	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed[6]	5 / 93 (5.38%)	5 / 93 (5.38%)	
occurrences (all)	7	9	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed[7]	1 / 93 (1.08%)	9 / 93 (9.68%)	
occurrences (all)	1	21	
Myalgia			
subjects affected / exposed[8]	3 / 93 (3.23%)	13 / 93 (13.98%)	
occurrences (all)	10	33	
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed[9]	1 / 93 (1.08%)	6 / 93 (6.45%)	
occurrences (all)	1	6	

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on the Exposed set, only on subjects with their symptom sheets completed

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on the Exposed set, only on subjects with their symptom sheets completed

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on the Exposed set, only on subjects with their symptom sheets completed

[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on the Exposed set, only on subjects with their symptom

sheets completed

[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on the Exposed set, only on subjects with their symptom sheets completed

[6] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on the Exposed set, only on subjects with their symptom sheets completed

[7] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on the Exposed set, only on subjects with their symptom sheets completed

[8] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on the Exposed set, only on subjects with their symptom sheets completed

[9] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on the Exposed set, only on subjects with their symptom sheets completed

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 February 2015	Rationale-As per CBER feedback on HT-hSBA validation plan, CBRE agreed to replace strain M01-0240364 with 96217. The minimum required safety follow-up after last vaccination was specified.In addition, need to obtain safety information at the planned last study contact was justified. Footnote for compostion of intervention was added for consistency.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported