Clinical trial results:
A Phase 2b, Randomized, Controlled, Observer-Blind, Multi-Center Study Assessing the Immunogenicity and Safety of GlaxoSmithKline (GSK) Biologicals' Meningococcal ABCWY Vaccine Administered at Different Schedules Compared to GSK Meningococcal group B vaccine, in Healthy Adolescents

Summary

EudraCT number	2013-002451-15
Trial protocol	FI PL
Global end of trial date	03 March 2016

Results information

Result version number	v1
This version publication date	18 May 2017
First version publication date	18 May 2017

Trial information

Trial identification

Sponsor protocol code	205215

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02212457
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	10 March 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	22 May 2015
Global end of trial reached?	Yes
Global end of trial date	03 March 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the non-inferiority of the Meningococcal (groups A, C, W and Y) oligosaccharide diphtheria CRM-197 conjugate combined with meningococcal (group B) multicomponent recombinant (MenABCWY) vaccine to that of the Meningococcal (group B) multicomponent recombinant adsorbed (rMenB +OMV) vaccine administered according to 0, 2 month schedule, as measured by hSBA GMTs against N. meningitidis serogroup B test strains1 at 1 month after the last meningococcal vaccination.

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 extended from the time a subject signed an informed consent until he or she completed the final study visit (Visit Month 13) or terminated the study early (whichever came first).

Background therapy: -

Evidence for comparator:

The comparator regimen of rMenB+OMV, Havrix Junior Monodose Havrix Monodose vaccines is already approved by the European Union (rMenB+OMV) and the United Kingdom (Havrix Junior Monodose and Havrix Monodose) for prophylactic use.

Actual start date of recruitment	21 August 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	Finland: 495
Country: Number of subjects enrolled	Poland: 433
Country: Number of subjects enrolled	United States: 135
Worldwide total number of subjects	1063
EEA total number of subjects	928

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)	289
Adolescents (12-17 years)	448
Adults (18-64 years)	326
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were recruited from 32 centers.

Pre-assignment

Screening details:

All subjects were included in the trial.

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:

The trial was designed as an observer-blind study. 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) were unaware which vaccine was administered.

Arms

Are arms mutually exclusive?	Yes
Arm title	rMenB_0_2 Group

Arm description:

Subjects received two injections of Bexsero™ vaccine at Visit Month 0 and Visit Month 2, Havrix® vaccine at Visit Month 6 and Visit Month 12 and saline placebo at Visit Month 1.

Arm type	Active comparator
Investigational medicinal product name	Bexsero®
Investigational medicinal product code	rMenB+OMV
Other name	GSK Meningococcal B Recombinant vaccine
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 milliliters (mL) dose of injectable suspension administered into the deltoid area of the non-dominant arm

Investigational medicinal product name	Havrix® Vaccine
Investigational medicinal product code	
Other name	Hepatitis A vaccine
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects between 1 and 15 years of age received one pediatric dose (0.5 mL) of Havrix® Junior Monodose® Vaccine (Hepatitis A virus antigen, 720 ELISA units/0.5 mL dose), administered in the deltoid muscle. Subjects 16 years of age or older received one adult dose (1.0 mL) of Havrix® Monodose® Vaccine (Hepatitis A virus antigen, 1440 ELISA units/1 mL dose of hepatitis A virus antigen), administered in the deltoid muscle.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	Saline solution
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL dose of injectable saline solution administered into the deltoid area of the non-dominant arm

Arm title	ABCWY_ 0_2 Group

Arm description:

Subjects received MenABCWY vaccine at Visit Month 0 and Visit Month 2, Havrix® vaccine at Visit Month 6 and Visit Month 12 and saline placebo at Visit Month 1.

Arm type	Experimental
Investigational medicinal product name	MenABCWY
Investigational medicinal product code	
Other name	GSK Meningococcal ABCWY Vaccine
Pharmaceutical forms	Powder and suspension for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL dose of injectable suspension administered into the deltoid area of the non-dominant arm

Investigational medicinal product name	Havrix® Vaccine
Investigational medicinal product code	
Other name	Hepatitis A vaccine
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects between 1 and 15 years of age received one pediatric dose (0.5 mL) of Havrix® Junior Monodose® Vaccine (Hepatitis A virus antigen, 720 ELISA units/0.5 mL dose), administered in the deltoid muscle. Subjects 16 years of age or older received one adult dose (1.0 mL) of Havrix® Monodose® Vaccine (Hepatitis A virus antigen, 1440 ELISA units/1 mL dose of hepatitis A virus antigen), administered in the deltoid muscle.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	Saline solution
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL dose of injectable saline solution administered into the deltoid area of the non-dominant arm

Arm title	ABCWY_0_1 Group

Arm description:

Subjects received MenABCWY vaccine at Visit Month 0 and Visit Month 1, Havrix® vaccine at Visit Month 2 and Visit Month 12 and saline placebo at Visit Month 6.

Arm type	Experimental
Investigational medicinal product name	MenABCWY
Investigational medicinal product code	
Other name	GSK Meningococcal ABCWY Vaccine
Pharmaceutical forms	Powder and suspension for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL dose of injectable suspension administered into the deltoid area of the non-dominant arm

Investigational medicinal product name	Havrix® Vaccine
Investigational medicinal product code	
Other name	Hepatitis A vaccine
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects between 1 and 15 years of age received one pediatric dose (0.5 mL) of Havrix® Junior Monodose® Vaccine (Hepatitis A virus antigen, 720 ELISA units/0.5 mL dose), administered in the deltoid muscle. Subjects 16 years of age or older received one adult dose (1.0 mL) of Havrix® Monodose® Vaccine (Hepatitis A virus antigen, 1440 ELISA units/1 mL dose of hepatitis A virus antigen), administered in the deltoid muscle.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	Saline solution
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL dose of injectable saline solution administered into the deltoid area of the non-dominant arm

Arm title	ABCWY_0_6 Group

Arm description:

Subjects received MenABCWY vaccine at Visit Month 0 and Visit Month 6, Havrix® vaccine at Visit Month 1 and Visit Month 12 and saline placebo at Visit Month 2.

Arm type	Experimental
Investigational medicinal product name	MenABCWY
Investigational medicinal product code	
Other name	GSK Meningococcal ABCWY Vaccine
Pharmaceutical forms	Powder and suspension for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL dose of injectable suspension administered into the deltoid area of the non-dominant arm

Investigational medicinal product name	Havrix® Vaccine
Investigational medicinal product code	
Other name	Hepatitis A vaccine
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects between 1 and 15 years of age received one pediatric dose (0.5 mL) of Havrix® Junior Monodose® Vaccine (Hepatitis A virus antigen, 720 ELISA units/0.5 mL dose), administered in the deltoid muscle. Subjects 16 years of age or older received one adult dose (1.0 mL) of Havrix® Monodose® Vaccine (Hepatitis A virus antigen, 1440 ELISA units/1 mL dose of hepatitis A virus antigen), administered in the deltoid muscle.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	Saline solution
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL dose of injectable saline solution administered into the deltoid area of the non-dominant arm

Arm title	ABCWY_0_11 Group

Arm description:

Subjects received MenABCWY vaccine at Visit Month 1 and Visit Month 12, Havrix® vaccine at Visit Month 0 and Visit Month 6 and saline placebo at Visit Month 2.

Arm type	Experimental
Investigational medicinal product name	MenABCWY
Investigational medicinal product code	
Other name	GSK Meningococcal ABCWY Vaccine
Pharmaceutical forms	Powder and suspension for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:	
0.5 mL dose of injectable suspension administered into the deltoid area of the non-dominant arm	
Investigational medicinal product name	Havrix® Vaccine
Investigational medicinal product code	
Other name	Hepatitis A vaccine
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
Subjects between 1 and 15 years of age received one pediatric dose (0.5 mL) of Havrix® Junior Monodose® Vaccine (Hepatitis A virus antigen, 720 ELISA units/0.5 mL dose), administered in the deltoid muscle. Subjects 16 years of age or older received one adult dose (1.0 mL) of Havrix® Monodose® Vaccine (Hepatitis A virus antigen, 1440 ELISA units/1 mL dose of hepatitis A virus antigen), administered in the deltoid muscle.	
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	Saline solution
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
0.5 mL dose of injectable saline solution administered into the deltoid area of the non-dominant arm	
Arm title	ABCWY_0_2_6 Group
Arm description:	
Subjects received MenABCWY vaccine at Visit Month 0, Visit Month 2 and Visit Month 6 and Havrix® vaccine at Visit Month 1 and Visit Month 12.	
Arm type	Experimental
Investigational medicinal product name	MenABCWY
Investigational medicinal product code	
Other name	GSK Meningococcal ABCWY Vaccine
Pharmaceutical forms	Powder and suspension for suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
0.5 mL dose of injectable suspension administered into the deltoid area of the non-dominant arm	
Investigational medicinal product name	Havrix® Vaccine
Investigational medicinal product code	
Other name	Hepatitis A vaccine
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
Subjects between 1 and 15 years of age received one pediatric dose (0.5 mL) of Havrix® Junior Monodose® Vaccine (Hepatitis A virus antigen, 720 ELISA units/0.5 mL dose), administered in the deltoid muscle. Subjects 16 years of age or older received one adult dose (1.0 mL) of Havrix® Monodose® Vaccine (Hepatitis A virus antigen, 1440 ELISA units/1 mL dose of hepatitis A virus antigen), administered in the deltoid muscle.	

Number of subjects in period 1	rMenB_0_2 Group	ABCWY_ 0_2 Group	ABCWY_0_1 Group
Started	228	232	157
Completed	209	211	141
Not completed	19	21	16
Consent withdrawn by subject	8	10	8

Adverse event, non-fatal	1	2	2
Unspecified	2	1	2
Lost to follow-up	6	7	4
Protocol deviation	2	1	-

Number of subjects in period 1	ABCWY_0_6 Group	ABCWY_0_11 Group	ABCWY_0_2_6 Group
Started	134	152	160
Completed	123	137	147
Not completed	11	15	13
Consent withdrawn by subject	6	5	4
Adverse event, non-fatal	2	-	1
Unspecified	1	-	1
Lost to follow-up	1	8	4
Protocol deviation	1	2	3

Baseline characteristics

Reporting groups	
Reporting group title	rMenB_0_2 Group
Reporting group description:	
Subjects received two injections of Bexsero™ vaccine at Visit Month 0 and Visit Month 2, Havrix® vaccine at Visit Month 6 and Visit Month 12 and saline placebo at Visit Month 1.	
Reporting group title	ABCWY_ 0_2 Group
Reporting group description:	
Subjects received MenABCWY vaccine at Visit Month 0 and Visit Month 2, Havrix® vaccine at Visit Month 6 and Visit Month 12 and saline placebo at Visit Month 1.	
Reporting group title	ABCWY_0_1 Group
Reporting group description:	
Subjects received MenABCWY vaccine at Visit Month 0 and Visit Month 1, Havrix® vaccine at Visit Month 2 and Visit Month 12 and saline placebo at Visit Month 6.	
Reporting group title	ABCWY_0_6 Group
Reporting group description:	
Subjects received MenABCWY vaccine at Visit Month 0 and Visit Month 6, Havrix® vaccine at Visit Month 1 and Visit Month 12 and saline placebo at Visit Month 2.	
Reporting group title	ABCWY_0_11 Group
Reporting group description:	
Subjects received MenABCWY vaccine at Visit Month 1 and Visit Month 12, Havrix® vaccine at Visit Month 0 and Visit Month 6 and saline placebo at Visit Month 2.	
Reporting group title	ABCWY_0_2_6 Group
Reporting group description:	
Subjects received MenABCWY vaccine at Visit Month 0, Visit Month 2 and Visit Month 6 and Havrix® vaccine at Visit Month 1 and Visit Month 12.	

Reporting group values	rMenB_0_2 Group	ABCWY_ 0_2 Group	ABCWY_0_1 Group
Number of subjects	228	232	157
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	56	73	39
Adolescents (12-17 years)	96	93	72
Adults (18-64 years)	76	66	46
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	14.5	14.2	14.4
standard deviation	± 3.09	± 3.17	± 3.01
Gender categorical Units: Subjects			
Female	130	119	101
Male	98	113	56

Reporting group values	ABCWY_0_6 Group	ABCWY_0_11 Group	ABCWY_0_2_6 Group
Number of subjects	134	152	160
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	35	39	47
Adolescents (12-17 years)	59	64	64
Adults (18-64 years)	40	49	49
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	14.4	14.5	14.3
standard deviation	± 3.06	± 3.1	± 3.16
Gender categorical			
Units: Subjects			
Female	76	89	96
Male	58	63	64

Reporting group values	Total		
Number of subjects	1063		
Age categorical			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	289		
Adolescents (12-17 years)	448		
Adults (18-64 years)	326		
From 65-84 years	0		
85 years and over	0		
Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	611		
Male	452		

End points

End points reporting groups

Reporting group title	rMenB_0_2 Group
Reporting group description:	
Subjects received two injections of Bexsero™ vaccine at Visit Month 0 and Visit Month 2, Havrix® vaccine at Visit Month 6 and Visit Month 12 and saline placebo at Visit Month 1.	
Reporting group title	ABCWY_ 0_2 Group
Reporting group description:	
Subjects received MenABCWY vaccine at Visit Month 0 and Visit Month 2, Havrix® vaccine at Visit Month 6 and Visit Month 12 and saline placebo at Visit Month 1.	
Reporting group title	ABCWY_0_1 Group
Reporting group description:	
Subjects received MenABCWY vaccine at Visit Month 0 and Visit Month 1, Havrix® vaccine at Visit Month 2 and Visit Month 12 and saline placebo at Visit Month 6.	
Reporting group title	ABCWY_0_6 Group
Reporting group description:	
Subjects received MenABCWY vaccine at Visit Month 0 and Visit Month 6, Havrix® vaccine at Visit Month 1 and Visit Month 12 and saline placebo at Visit Month 2.	
Reporting group title	ABCWY_0_11 Group
Reporting group description:	
Subjects received MenABCWY vaccine at Visit Month 1 and Visit Month 12, Havrix® vaccine at Visit Month 0 and Visit Month 6 and saline placebo at Visit Month 2.	
Reporting group title	ABCWY_0_2_6 Group
Reporting group description:	
Subjects received MenABCWY vaccine at Visit Month 0, Visit Month 2 and Visit Month 6 and Havrix® vaccine at Visit Month 1 and Visit Month 12.	

Primary: Human Serum Bactericidal Assay (hSBA) Geometric Mean Titers (GMTs) against N. meningitidis serogroup B test strains

End point title	Human Serum Bactericidal Assay (hSBA) Geometric Mean Titers (GMTs) against N. meningitidis serogroup B test strains[1]
End point description:	
The non-inferiority of the Meningococcal (groups A, C, W and Y) oligosaccharide diphtheria CRM-197 conjugate combined with meningococcal (group B) multicomponent recombinant (MenABCWY) vaccine to Meningococcal (group B) multicomponent recombinant adsorbed (Bexsero™) vaccine, administered according to 0, 2 month schedule, as measured by hSBA GMTs against N.meningitidis serogroup B test strains at 1 month after the last meningococcal vaccination, is reported. The test strains assessed were Meningitis B NZ98/254 Ab, Meningitis B M14459 Ab, Meningitis B M07-0241084 Ab and Meningitis B 96217 Ab. This outcome measure was evaluated only in the rMenB_0_2 and ABCWY_ 0_2 Groups. The analysis was performed on the PPS (Per Protocol Set) Month 3 population, which included all subjects in the All Enrolled Set who received a study vaccination and provided evaluable serum samples at pre- (Visit Month 0) and at least one post-vaccination (Visit Month 3).	
End point type	Primary
End point timeframe:	
At baseline (Month 0) and 1 month after the last meningococcal vaccination (Month 3)	

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: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

End point values	rMenB_0_2 Group	ABCWY_ 0_2 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	150	158		
Units: Titers				
geometric mean (confidence interval 95%)				
M14459 strain (Month 0) [N=155;147]	1.31 (1.09 to 1.57)	1.28 (1.07 to 1.53)		
M14459 strain (Month 3) [N=158;150]	15.78 (12 to 22)	11.64 (8.61 to 16)		
M07-0241084 strain (Month 0) [N=151;148]	2.16 (1.61 to 2.89)	2.12 (1.6 to 2.82)		
M07-0241084 strain (Month 3) [N=154;150]	11.56 (8.86 to 15)	8.19 (6.31 to 11)		
96217 strain (Month 0) [N=152;143]	2.36 (1.7 to 3.28)	2.93 (2.13 to 4.03)		
96217 strain (Month 3) [N=156;149]	229.29 (179 to 294)	150.82 (118 to 192)		
NZ98/254 strain (Month 0) [N=154;147]	1.15 (0.95 to 1.39)	1.27 (1.06 to 1.53)		
NZ98/254 strain (Month 3) [N=157;150]	24.31 (18 to 32)	11.95 (9.1 to 16)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description:	
Non-inferiority response against N. meningitidis serogroup B test strain M14459 of the MenABCWY vaccine to that of the Bexsero™ vaccine, administered according to 0, 2 month schedule.	
Comparison groups	rMenB_0_2 Group v ABCWY_ 0_2 Group
Number of subjects included in analysis	308
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
Method	ANCOVA
Parameter estimate	Between Group Ratio
Point estimate	0.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.54
upper limit	1.03

Notes:

[2] - Non-inferiority criterion was met if at 1 month after the second meningococcal vaccination (Visit Month 3) the lower limit of the two-sided 95% confidence interval for the between-group ratios of GMTs (ABCWY_0_2 versus rMenB_0_2) was greater than 0.5 for each of the four serogroup B test strains.

Statistical analysis title	Statistical analysis 2
Statistical analysis description:	
Non-inferiority response against N. meningitidis serogroup B test strain M07-0241084 of the MenABCWY vaccine to that of the Bexsero™ vaccine, administered according to 0, 2 month schedule.	
Comparison groups	rMenB_0_2 Group v ABCWY_ 0_2 Group

Number of subjects included in analysis	308
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
Method	ANCOVA
Parameter estimate	Between Group Ratio
Point estimate	0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.53
upper limit	0.92

Notes:

[3] - Non-inferiority criterion was met if at 1 month after the second meningococcal vaccination (Visit Month 3)the lower limit of the two-sided 95% confidence interval for the between-group ratios of GMTs (ABCWY_0_2 versus rMenB_0_2) was greater than 0.5 for each of the four serogroup B test strains.

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

Non-inferiority response against N. meningitidis serogroup B test strain 96217 of the MenABCWY vaccine to that of the Bexsero™ vaccine, administered according to 0, 2 month schedule.

Comparison groups	rMenB_0_2 Group v ABCWY_ 0_2 Group
Number of subjects included in analysis	308
Analysis specification	Pre-specified
Analysis type	non-inferiority[4]
Method	ANCOVA
Parameter estimate	Between Group Ratio
Point estimate	0.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.51
upper limit	0.85

Notes:

[4] - Non-inferiority criterion was met if at 1 month after the second meningococcal vaccination (Visit Month 3) the lower limit of the two-sided 95% confidence interval for the between-group ratios of GMTs (ABCWY_0_2 versus rMenB_0_2) was greater than 0.5 for each of the four serogroup B test strains.

Statistical analysis title	Statistical analysis 4

Statistical analysis description:

Non-inferiority response against N. meningitidis serogroup B test strain NZ98/254 of the MenABCWY vaccine to that of the Bexsero™ vaccine, administered according to 0, 2 month schedule.

Comparison groups	rMenB_0_2 Group v ABCWY_ 0_2 Group
Number of subjects included in analysis	308
Analysis specification	Pre-specified
Analysis type	non-inferiority[5]
Method	ANCOVA
Parameter estimate	Between Group Ratio
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.37
upper limit	0.66

Notes:

[5] - Non-inferiority criterion was met if at 1 month after the second meningococcal vaccination (Visit Month 3) the lower limit of the two-sided 95% confidence interval for the between-group ratios of GMTs (ABCWY_0_2 versus rMenB_0_2) was greater than 0.5 for each of the four serogroup B test strains.

Secondary: hSBA GMTs against N. meningitidis serogroup B test strains

End point title	hSBA GMTs against N. meningitidis serogroup B test strains[6]

End point description:

The immunogenicity of MenABCWY vaccine, administered according to 0, 2, 6 months schedule is compared with those administered according to 0, 6 months schedule, as measured by hSBA GMTs against N. meningitidis serogroup B test strains at 1 month after the last meningococcal vaccination. The test strains assessed were Meningitis B NZ98/254 Ab, Meningitis B M14459 Ab, Meningitis B M07-0241084 Ab and Meningitis B 96217 Ab. This outcome measure was evaluated only in the ABCWY_ 0_2 and ABCWY_0_2_6 Groups. The analysis was performed on the Full analysis set (FAS) 1 month after the last meningococcal vaccination. 1 month post last meningococcal vaccination corresponds to Month 3 for ABCWY_0_2 Group and Month 7 for ABCWY_0_2_6 Group.

End point type	Secondary

End point timeframe:

At baseline (Month 0) and 1 month after the last meningococcal vaccination (Month 3/Month 7)

Notes:

[6] - 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: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

End point values	ABCWY_ 0_2 Group	ABCWY_0_2_6 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	212	151		
Units: Titers				
geometric mean (confidence interval 95%)				
M14459 strain (Month 0) [N=207;151]	1.21 (1.07 to 1.37)	1.12 (0.98 to 1.28)		
M14459 strain (Month 3/Month 7) [N=211;151]	12.17 (9.6 to 15)	27.09 (21 to 35)		
M07-0241084 strain (Month 0) [N=201;145]	2.36 (1.85 to 3.01)	2.05 (1.58 to 2.67)		
M07-0241084 strain (Month 3/Month 7) [N=206;148]	8.91 (7.1 to 11)	18.03 (14 to 23)		
96217 strain (Month 0) [N=205;146]	2.31 (1.75 to 3.06)	2.28 (1.68 to 3.07)		
96217 strain (Month 3/Month 7) [N=210;150]	174.27 (142 to 215)	298.76 (239 to 374)		
NZ98/254 strain (Month 0) [N=208;151]	1.24 (1.09 to 1.41)	1.07 (0.93 to 1.23)		
NZ98/254 strain (Month 3/Month 7) [N=212;151]	12.57 (9.81 to 16)	17.55 (13 to 23)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentages of subjects with hSBA titers ≥ Lower Limit of Quantitation (LLQ) against N. meningitidis serogroup B test strains

End point title	Percentages of subjects with hSBA titers ≥ Lower Limit of Quantitation (LLQ) against N. meningitidis serogroup B test strains[7]

End point description:

The immunogenicity of MenABCWY vaccine, administered according to 0, 2, 6 month schedule, was compared with those, administered according to 0, 6 month schedule, as measured by the percentages of subjects with hSBA titers ≥ LLQ (≥ 5, ≥ 8 and ≥ 16) against N. meningitidis serogroup B test strains at 1 month after the last meningococcal vaccination.
The analysis was performed on FAS 1 month after the last meningococcal vaccination population, which included all subjects in the All Enrolled Set who received a meningococcal vaccination and provided evaluable serum samples at one month after the last meningococcal vaccination and whose result was available for at least one A, C, W and Y serogroup or serogroup B strain.
Note: The value of the LLQ will be determined after assay validation and the cut-offs mentioned above were selected for use.

End point type	Secondary

End point timeframe:

At baseline (Month 0) and 1 month after the last meningococcal vaccination (Month 3/Month 7)

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The results in this study were tabulated by age group and study period. Hence for each related endpoint, they are presented for only the respective groups in the baseline period, while the results for multiple endpoints account for all baseline groups.

End point values	ABCWY_ 0_2 Group	ABCWY_0_2_6 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	212	151		
Units: Percentages of subjects				
number (confidence interval 95%)				
M14459 strain; ≥ 5 (Month 0) [N=207;151]	8 (4.5 to 12.2)	3 (1.1 to 7.6)		
M14459 strain; ≥ 8 (Month 0) [N=207;151]	5 (2.7 to 9.3)	2 (0.41 to 5.7)		
M14459 strain; ≥ 16 (Month 0) [N=207;151]	2 (0.5 to 4.9)	1 (0.16 to 4.7)		
M14459 strain; ≥ 5 (Month 3/Month 7) [N=211;151]	75 (69 to 81)	94 (89 to 97.2)		
M14459 strain; ≥ 8 (Month 3/Month 7) [N=211;151]	70 (63.5 to 76.2)	89 (83.4 to 93.8)		
M14459 strain; ≥ 16 (Month 3/Month 7)[N=211;151]	53 (45.6 to 59.5)	73 (65 to 79.8)		
M07-0241084 strain ≥ 5 (Month 0) [N=201;145]	27 (21.3 to 34.1)	21 (14.4 to 28.2)		
M07-0241084 strain ≥ 8 (Month 0) [N=201;145]	20 (14.6 to 26.1)	19 (13.2 to 26.7)		
M07-0241084 strain ≥ 16 (Month 0) [N=201;145]	14 (9.5 to 19.5)	14 (9.2 to 21.3)		
M07-0241084 strain ≥5(Month 3/Month 7)[N=206;148]	71 (64.7 to 77.4)	82 (75.3 to 88.2)		
M07-0241084 strain ≥8(Month 3/Month 7)[N=206;148]	56 (48.8 to 62.7)	79 (71.6 to 85.3)		
M07-0241084 strain≥16(Month 3/Month 7)[N=206;148]	33 (26.6 to 39.9)	58 (49.7 to 66.2)		
96217 strain; ≥ 5 (Month 0) [N=205;146]	35 (28.1 to 41.6)	29 (22.2 to 37.6)		
96217 strain; ≥ 8 (Month 0) [N=205;146]	30 (24 to 37)	28 (21 to 36.1)		
96217 strain; ≥ 16 (Month 0) [N=205;146]	17 (12.2 to 22.9)	18 (12 to 25)		

96217 strain; ≥ 5 (Month 3/Month 7) [N=210;150]	98 (94.5 to 99.2)	99 (96.3 to 99.98)		
96217 strain; ≥ 8 (Month 3/Month 7) [N=210;150]	97 (93.3 to 98.6)	99 (96.3 to 99.98)		
96217 strain; ≥ 16 (Month 3/Month 7) [N=210;150]	95 (91.4 to 97.7)	99 (96.3 to 99.98)		
NZ98/254 strain ≥ 5 (Month 0) [N= 208;151]	8 (4.5 to 12.2)	3 (0.7 to 6.6)		
NZ98/254 strain ≥ 8 (Month 0) [N= 208;151]	6 (3.4 to 10.5)	2 (0.41 to 5.7)		
NZ98/254 strain ≥ 16 (Month 0) [N= 208;151]	5 (2.7 to 9.3)	1 (0.02 to 3.6)		
NZ98/254 strain ≥ 5(Month 3/Month 7) [N=212;151]	77 (70.6 to 82.4)	82 (75.1 to 87.9)		
NZ98/254 strain ≥ 8 (Month 3/Month 7) [N=212;151]	64 (57.3 to 70.6)	75 (67.1 to 81.5)		
NZ98/254 strain ≥ 16 (Month 3/Month 7)[N=212;151]	47 (40.3 to 54.1)	57 (48.7 to 65)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any and Grade 3 solicited local or systemic adverse events (AEs) and other indicators of reactogenicity

End point title	Number of subjects reporting any and Grade 3 solicited local or systemic adverse events (AEs) and other indicators of reactogenicity

End point description:

The number of subjects with any and Grade 3 solicited local or systemic AEs and other indicators of reactogenicity within 30 minutes after each vaccination.
Assessed solicited local symptoms were: pain, erythema and induration. Assessed solicited systemic symptoms were: fatigue, headache, myalgia, arthralgia, loss of appetite, nausea, chills, and fever (body temperature ≥38.0°C). Other solicited data included: Prevention of Pain and/or Fever and Treatment of Pain and/or Fever. Any = occurrence of the symptom regardless of intensity grade. Grade 3 symptom = symptom that prevented normal activity.
The analysis was performed on the Solicited Safety Set population, which included all screened subjects who provided informed consent, demographic and/or baseline screening assessments, regardless of the subject's randomization and treatment status in the study, received a Subject ID and a study vaccination, and who provided post-vaccination reactogenicity data.

End point type	Secondary

End point timeframe:

Within 30 minutes after vaccination

End point values	rMenB_0_2 Group	ABCWY_ 0_2 Group	ABCWY_0_1 Group	ABCWY_0_6 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	228	232	155	134
Units: Subjects				
Any Induration (1st) [N=217,219,146,128,143,151]	0	0	0	0
Grade3 Induration(1st)[N=217,219,146,128,14	0	0	0	0

Any Induration (2nd) [N=215,217,150,125,144,151]	0	0	0	0
Grade3 Induration(2nd)[N=215,217,150,125,14	0	0	0	0
Any Induration (3rd) [N=212,219,146,125,141,151]	0	0	0	0
Grade3 Induration(3rd)[N=212,219,146,125,14	0	0	0	0
Any Induration (4th) [N=212,214,141,124,138,152]	0	0	0	0
Grade3 Induration(4th)[N=212,214,141,124,13	0	0	0	0
Any Induration (5th) [N=207,206,141,122,134,149]	0	0	0	0
Grade3 Induration(5th)[N=207,206,141,122,13	0	0	0	0
Any Erythema (1st) [N=217,219,146,128,143,151]	1	0	0	0
Grade 3 Erythema(1st) [N=217,219,146,128,143,151]	0	0	0	0
Any Erythema (2nd) [N=215,217,150,125,144,151]	2	0	0	1
Grade 3 Erythema (2nd)[N=215,217,150,125,144,151]	0	0	0	0
Any Erythema (3rd) [N=212,219,146,125,141,151]	0	1	0	1
Grade 3 Erythema (3rd) [N=212,219,146,125,141,151]	0	0	0	0
Any Erythema (4th) [N=212,214,141,124,138,152]	0	1	0	0
Grade 3 Erythema(4th) [N=212,214,141,124,138,152]	0	0	0	0
Any Erythema (5th) [N=206,206,141,122,133,149]	0	0	0	0
Grade 3 Erythema(5th) [N=206,206,141,122,133,149]	0	0	0	0
Any Pain(1st) [N=228,231,155,134,151,159]	19	4	12	8
Grade 3 Pain (1st) [N=228,231,155,134,151,159]	0	0	0	0
Any Pain (2nd) [N=216,221,150,129,145,153]	10	12	11	9
Grade 3 Pain (2nd) [N=216,221,150,129,145,153]	0	0	0	0
Any Pain (3rd) [N=213,219,146,126,141,152]	10	11	8	7
Grade 3 Pain (3rd) [N=213,219,146,126,141,152]	0	0	0	0
Any Pain (4th) [N=212,214,141,124,138,152]	28	22	7	14
Grade 3 Pain (4th) [N=212,214,141,124,138,152]	0	0	0	0
Any Pain (5th) [N=207,206,141,122,133,149]	19	16	12	15
Grade 3 Pain (5th) [N=207,206,141,122,133,149]	0	0	0	0
Any Nausea (1st) [N=228,231,155,134,151,158]	0	0	2	1
Grade 3 Nausea (1st) [N=228,231,155,134,151,159]	0	0	0	0
Any Nausea (2nd) [N=216,221,150,129,145,153]	2	0	1	1

Grade 3 Nausea (2nd) [N=216,221,150,129,145,153]	0	0	0	0
Any Nausea (3rd) [N=213,219,146,126,141,152]	2	0	2	0
Grade 3 Nausea (3rd) [N=213,219,146,126,141,152]	0	0	0	0
Any Nausea (4th) [N=212,214,141,124,138,152]	2	0	2	0
Grade 3 Nausea (4th) [N=212,214,141,124,138,152]	0	0	0	0
Any Nausea (5th) [N=207,206,141,122,134,149]	1	0	3	1
Grade 3 Nausea (5th) [N=207,206,141,122,134,149]	0	0	0	0
Any Fatigue (1st) [N=228,231,155,134,151,158]	4	6	6	1
Grade 3 Fatigue (1st) [N=228,231,155,134,151,158]	0	0	0	0
Any Fatigue (2nd) [N=216,221,150,129,145,153]	4	3	1	1
Grade 3 Fatigue (2nd) [N=216,221,150,129,145,153]	0	0	0	0
Any Fatigue (3rd) [N=213,219,146,126,141,152]	2	4	0	1
Grade 3 Fatigue(3rd) [N=213,219,146,126,141,152]	0	0	0	1
Any Fatigue (4th) [N=212,214,141,124,138,152]	2	1	1	0
Grade 3 Fatigue (4th) [N=212,214,141,124,138,152]	0	0	0	0
Any Fatigue (5th) [N=207,206,141,122,134,149]	1	2	1	3
Grade 3 Fatigue (5th) [N=207,206,141,122,134,149]	0	0	0	0
Any Myalgia (1st) [N=228,231,155,134,151,158]	0	1	0	0
Grade 3 Myalgia (1st) [N=228,231,155,134,151,158]	0	0	0	0
Any Myalgia (2nd) [N=216,221,150,129,145,153]	0	0	1	0
Grade 3 Myalgia (2nd) [N=216,221,150,129,145,153]	0	0	0	0
Any Myalgia (3rd) [N=213,219,146,126,141,152]	0	0	0	1
Grade 3 Myalgia (3rd) [N=213,219,146,126,141,152]	0	0	0	0
Any Myalgia (4th) [N=212,214,141,124,138,152]	0	0	0	0
Grade 3 Myalgia (4th) [N=212,214,141,124,138,152]	0	0	0	0
Any Myalgia (5th) [N=207,206,141,122,134,149]	0	4	1	0
Grade 3 Myalgia (5th) [N=207,206,141,122,134,149]	0	0	0	0
Any Arthralgia (1st) [N=228,231,155,134,151,158]	0	0	0	0
Grade3 Arthralgia(1st)[N=228,231,155,134,151	0	0	0	0
Any Arthralgia (2nd) [N=216,221,150,129,145,153]	0	0	0	0
Grade3 Arthralgia(2nd)[N=216,221,150,129,14	0	0	0	0

Any Arthralgia (3rd) [N=213,219,146,126,141,152]	0	0	0	0
Grade3 Arthralgia(3rd)[N=213,219,146,126,141	0	0	0	0
Any Arthralgia (4th) [N=212,214,141,124,138,152]	0	0	0	0
Grade3 Arthralgia(4th)[N=212,214,141,124,138	0	0	0	0
Any Arthralgia (5th) [N=207,206,141,122,134,149]	0	0	0	0
Grade3 Arthralgia(5th)[N=207,206,141,122,134	0	0	0	0
Any Headache (1st) [N=228,231,155,134,151,158]	2	3	1	1
Grade 3 Headache(1st) [N=228,231,155,134,151,158]	0	0	0	0
Any Headache (2nd) [N=216,221,150,129,145,153]	3	1	2	1
Grade 3 Headache (2nd)[N=216,221,150,129,145,153]	0	0	0	0
Any Headache (3rd) [N=213,219,146,126,141,152]	2	1	2	0
Grade 3 Headache(3rd) [N=213,219,146,126,141,152]	0	0	0	0
Any Headache (4th) [N=212,214,141,124,138,152]	3	2	0	0
Grade 3 Headache (4th)[N=212,214,141,124,138,152]	0	0	0	0
Any Headache (5th) [N=207,206,141,122,134,149]	2	1	0	0
Grade 3 Headache(5th) [N=207,206,141,122,134,149]	0	0	0	0
Any Chills (1st) [N=228,231,155,134,151,158]	0	1	1	0
Grade 3 Chills (1st) [N=228,231,155,134,151,158]	0	0	0	0
Any Chills (2nd) [N=216,221,150,129,145,153]	1	1	1	1
Grade 3 Chills (2nd) [N=216,221,150,129,145,153]	0	0	0	0
Any Chills (3rd) [N=213,219,146,126,141,152]	1	1	0	0
Grade 3 Chills (3rd) [N=213,219,146,126,141,152]	0	0	0	0
Any Chills (4th) [N=212,214,141,124,138,152]	1	1	0	0
Grade 3 Chills (4th) [N=212,214,141,124,138,152]	0	0	0	0
Any Chills (5th) [N=207,206,141,122,134,149]	1	1	0	0
Grade 3 Chills (5th) [N=207,206,141,122,134,149]	0	0	0	0
Any Appetite Loss(1)[N=228,231,155,134,151,158]	0	0	0	0
Grade3AppetiteLoss(1)[N=228,231,155, 134,151,158]	0	0	0	0
Any Appetite Loss(2)[N=216,221,150,129,145,153]	0	0	0	0
Grade3AppetiteLoss(2)[N=216,221,150, 129,145,153]	0	0	0	0
Any Appetite Loss(3)[N=213,219,146,126,141,152]	0	0	0	0

Grade3AppetiteLoss(3)[N=213,219,146,126,141,152]	0	0	0	0
Any Appetite Loss(4)[N=212,214,141,124,138,152]	0	0	0	0
Grade3AppetiteLoss(4)[N=212,214,141,124,138,152]	0	0	0	0
Any Appetite Loss(5)[N=207,206,141,122,134,149]	0	0	0	0
Grade3AppetiteLoss(5)[N=207,206,141,122,134,149]	0	0	0	0
Fever (1st) [N=228,232,155,133,151,158]	0	0	0	0
Fever (2nd) [N=216,221,150,128,145,153]	0	0	0	0
Fever (3rd) [N=213,218,146,125,141,152]	0	0	0	0
Fever (4th) [N=211,214,140,124,137,152]	0	0	0	0
Fever (5th) [N=207,206,141,122,134,149]	0	0	0	0
Pain/Fever prevention(1)N=228,232,155,134,151,1	0	0	0	0
Pain/Fever prevention(2)N=216,221,150,129,145,1	0	2	0	0
Pain/Fever prevention(3)N=213,219,146,126,141,1	1	0	0	0
Pain/Fever prevention(4)N=211,214,141,124,138,1	0	0	0	0
Pain/Fever prevention(5)N=207,206,141,122,134,1	0	0	0	0
Pain/Fever treatment(1)N=227,232,155,134,151,1	0	0	1	0
Pain/Fever treatment(2)N=216,221,150,129,145,1	1	0	0	0
Pain/Fever treatment(3)N=213,219,146,126,141,1	0	0	0	0
Pain/Fever treatment(4)N=212,214,141,124,138,1	0	1	0	0
Pain/Fever treatment(5)N=207,206,141,122,134,1	0	0	0	0

End point values	ABCWY_0_11 Group	ABCWY_0_2_6 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	151	159		
Units: Subjects				
Any Induration (1st) [N=217,219,146,128,143,151]	0	0		
Grade3 Induration(1st)[N=217,219,146,128,14	0	0		
Any Induration (2nd) [N=215,217,150,125,144,151]	0	0		
Grade3 Induration(2nd)[N=215,217,150,125,14	0	0		
Any Induration (3rd) [N=212,219,146,125,141,151]	0	0		
Grade3 Induration(3rd)[N=212,219,146,125,14	0	0		

Any Induration (4th) [N=212,214,141,124,138,152]	0	0		
Grade3 Induration(4th)[N=212,214,141,124,13	0	0		
Any Induration (5th) [N=207,206,141,122,134,149]	0	0		
Grade3 Induration(5th)[N=207,206,141,122,13	0	0		
Any Erythema (1st) [N=217,219,146,128,143,151]	1	0		
Grade 3 Erythema(1st) [N=217,219,146,128,143,151]	0	0		
Any Erythema (2nd) [N=215,217,150,125,144,151]	0	0		
Grade 3 Erythema (2nd)[N=215,217,150,125,144,151]	0	0		
Any Erythema (3rd) [N=212,219,146,125,141,151]	0	0		
Grade 3 Erythema (3rd) [N=212,219,146,125,141,151]	0	0		
Any Erythema (4th) [N=212,214,141,124,138,152]	0	1		
Grade 3 Erythema(4th) [N=212,214,141,124,138,152]	0	0		
Any Erythema (5th) [N=206,206,141,122,133,149]	0	0		
Grade 3 Erythema(5th) [N=206,206,141,122,133,149]	0	0		
Any Pain(1st) [N=228,231,155,134,151,159]	17	13		
Grade 3 Pain (1st) [N=228,231,155,134,151,159]	0	0		
Any Pain (2nd) [N=216,221,150,129,145,153]	14	9		
Grade 3 Pain (2nd) [N=216,221,150,129,145,153]	0	0		
Any Pain (3rd) [N=213,219,146,126,141,152]	5	13		
Grade 3 Pain (3rd) [N=213,219,146,126,141,152]	0	0		
Any Pain (4th) [N=212,214,141,124,138,152]	8	17		
Grade 3 Pain (4th) [N=212,214,141,124,138,152]	0	0		
Any Pain (5th) [N=207,206,141,122,133,149]	13	12		
Grade 3 Pain (5th) [N=207,206,141,122,133,149]	0	0		
Any Nausea (1st) [N=228,231,155,134,151,158]	2	2		
Grade 3 Nausea (1st) [N=228,231,155,134,151,159]	0	0		
Any Nausea (2nd) [N=216,221,150,129,145,153]	0	0		
Grade 3 Nausea (2nd) [N=216,221,150,129,145,153]	0	0		
Any Nausea (3rd) [N=213,219,146,126,141,152]	0	1		
Grade 3 Nausea (3rd) [N=213,219,146,126,141,152]	0	0		
Any Nausea (4th) [N=212,214,141,124,138,152]	1	0		

Grade 3 Nausea (4th) [N=212,214,141,124,138,152]	0	0		
Any Nausea (5th) [N=207,206,141,122,134,149]	0	1		
Grade 3 Nausea (5th) [N=207,206,141,122,134,149]	0	0		
Any Fatigue (1st) [N=228,231,155,134,151,158]	2	1		
Grade 3 Fatigue (1st) [N=228,231,155,134,151,158]	0	0		
Any Fatigue (2nd) [N=216,221,150,129,145,153]	2	0		
Grade 3 Fatigue (2nd) [N=216,221,150,129,145,153]	0	0		
Any Fatigue (3rd) [N=213,219,146,126,141,152]	1	2		
Grade 3 Fatigue(3rd) [N=213,219,146,126,141,152]	0	0		
Any Fatigue (4th) [N=212,214,141,124,138,152]	1	3		
Grade 3 Fatigue (4th) [N=212,214,141,124,138,152]	0	0		
Any Fatigue (5th) [N=207,206,141,122,134,149]	1	1		
Grade 3 Fatigue (5th) [N=207,206,141,122,134,149]	0	0		
Any Myalgia (1st) [N=228,231,155,134,151,158]	0	0		
Grade 3 Myalgia (1st) [N=228,231,155,134,151,158]	0	0		
Any Myalgia (2nd) [N=216,221,150,129,145,153]	3	1		
Grade 3 Myalgia (2nd) [N=216,221,150,129,145,153]	0	0		
Any Myalgia (3rd) [N=213,219,146,126,141,152]	0	0		
Grade 3 Myalgia (3rd) [N=213,219,146,126,141,152]	0	0		
Any Myalgia (4th) [N=212,214,141,124,138,152]	1	0		
Grade 3 Myalgia (4th) [N=212,214,141,124,138,152]	0	0		
Any Myalgia (5th) [N=207,206,141,122,134,149]	1	0		
Grade 3 Myalgia (5th) [N=207,206,141,122,134,149]	0	0		
Any Arthralgia (1st) [N=228,231,155,134,151,158]	0	0		
Grade3 Arthralgia(1st)[N=228,231,155,134,151	0	0		
Any Arthralgia (2nd) [N=216,221,150,129,145,153]	0	0		
Grade3 Arthralgia(2nd)[N=216,221,150,129,14	0	0		
Any Arthralgia (3rd) [N=213,219,146,126,141,152]	0	0		
Grade3 Arthralgia(3rd)[N=213,219,146,126,141	0	0		
Any Arthralgia (4th) [N=212,214,141,124,138,152]	0	0		
Grade3 Arthralgia(4th)[N=212,214,141,124,138	0	0		

Any Arthralgia (5th) [N=207,206,141,122,134,149]	0	0		
Grade3 Arthralgia(5th)[N=207,206,141,122,134	0	0		
Any Headache (1st) [N=228,231,155,134,151,158]	1	0		
Grade 3 Headache(1st) [N=228,231,155,134,151,158]	0	0		
Any Headache (2nd) [N=216,221,150,129,145,153]	1	1		
Grade 3 Headache (2nd)[N=216,221,150,129,145,153]	0	0		
Any Headache (3rd) [N=213,219,146,126,141,152]	1	1		
Grade 3 Headache(3rd) [N=213,219,146,126,141,152]	0	0		
Any Headache (4th) [N=212,214,141,124,138,152]	1	1		
Grade 3 Headache (4th)[N=212,214,141,124,138,152]	0	0		
Any Headache (5th) [N=207,206,141,122,134,149]	0	1		
Grade 3 Headache(5th) [N=207,206,141,122,134,149]	0	0		
Any Chills (1st) [N=228,231,155,134,151,158]	2	2		
Grade 3 Chills (1st) [N=228,231,155,134,151,158]	0	0		
Any Chills (2nd) [N=216,221,150,129,145,153]	0	0		
Grade 3 Chills (2nd) [N=216,221,150,129,145,153]	0	0		
Any Chills (3rd) [N=213,219,146,126,141,152]	0	0		
Grade 3 Chills (3rd) [N=213,219,146,126,141,152]	0	0		
Any Chills (4th) [N=212,214,141,124,138,152]	0	0		
Grade 3 Chills (4th) [N=212,214,141,124,138,152]	0	0		
Any Chills (5th) [N=207,206,141,122,134,149]	0	0		
Grade 3 Chills (5th) [N=207,206,141,122,134,149]	0	0		
Any Appetite Loss(1)[N=228,231,155,134,151,158]	0	0		
Grade3AppetiteLoss(1)[N=228,231,155, 134,151,158]	0	0		
Any Appetite Loss(2)[N=216,221,150,129,145,153]	0	0		
Grade3AppetiteLoss(2)[N=216,221,150, 129,145,153]	0	0		
Any Appetite Loss(3)[N=213,219,146,126,141,152]	0	0		
Grade3AppetiteLoss(3)[N=213,219,146, 126,141,152]	0	0		
Any Appetite Loss(4)[N=212,214,141,124,138,152]	0	0		
Grade3AppetiteLoss(4)[N=212,214,141, 124,138,152]	0	0		
Any Appetite Loss(5)[N=207,206,141,122,134,149]	0	0		

Grade3AppetiteLoss(5)[N=207,206,141,122,134,149]	0	0		
Fever (1st) [N=228,232,155,133,151,158]	0	0		
Fever (2nd) [N=216,221,150,128,145,153]	0	0		
Fever (3rd) [N=213,218,146,125,141,152]	0	0		
Fever (4th) [N=211,214,140,124,137,152]	0	0		
Fever (5th) [N=207,206,141,122,134,149]	0	0		
Pain/Fever prevention(1)N=228,232,155,134,151,1	0	0		
Pain/Fever prevention(2)N=216,221,150,129,145,1	0	0		
Pain/Fever prevention(3)N=213,219,146,126,141,1	0	0		
Pain/Fever prevention(4)N=211,214,141,124,138,1	0	0		
Pain/Fever prevention(5)N=207,206,141,122,134,1	0	0		
Pain/Fever treatment(1)N=227,232,155,134,151,1	0	0		
Pain/Fever treatment(2)N=216,221,150,129,145,1	0	1		
Pain/Fever treatment(3)N=213,219,146,126,141,1	0	0		
Pain/Fever treatment(4)N=212,214,141,124,138,1	0	0		
Pain/Fever treatment(5)N=207,206,141,122,134,1	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any and Grade 3 solicited local or systemic adverse events (AEs) and other indicators of reactogenicity

End point title	Number of subjects reporting any and Grade 3 solicited local or systemic adverse events (AEs) and other indicators of reactogenicity

End point description:

The number of subjects with any or Grade 3 solicited local or systemic AEs and other indicators of reactogenicity from Day 1 (6 hours) to Day 7 after each vaccination is reported.
Assessed solicited local symptoms were: pain, erythema and induration. Assessed solicited systemic symptoms were: fatigue, headache, myalgia, arthralgia, loss of appetite, nausea, chills, and fever (body temperature ≥38.0°C). Other solicited data included: Prevention of Pain and/or Fever and Treatment of Pain and/or Fever. Any = occurrence of the symptom regardless of intensity grade. Grade 3 symptom = symptom that prevented normal activity.
The analysis was performed on the Solicited Safety Set population, which included all screened subjects who provided informed consent, demographic and/or baseline screening assessments, regardless of the subject's randomization and treatment status in the study, received a Subject ID and a study vaccination, and who provided post-vaccination reactogenicity data.

End point type	Secondary

End point timeframe:

From Day 1 (6 hours) to Day 7 after each vaccination

End point values	rMenB_0_2 Group	ABCWY_ 0_2 Group	ABCWY_0_1 Group	ABCWY_0_6 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	228	231	155	134
Units: Subjects				
Any AE [N= 228, 231, 155, 134, 151, 159]	224	227	153	131
Any Local AE [N= 228, 231, 155, 134, 151, 159]	221	225	148	129
Any Systemic AE [N= 228, 231, 155, 134, 151, 159]	201	201	143	117
Any Pain (1st) [N=227,231,154,134,151,159]	213	223	142	126
Grade 3 Pain (1st) [N=227,231,154,134,151,159]	9	13	2	10
Any Pain (2nd) [N=214,216,150,128,144,151]	32	34	122	41
Grade 3 Pain (2nd) [N=214,216,150,128,144,151]	0	1	5	0
Any Pain (3rd) [N=212,217,144,125,138,150]	193	185	38	26
Grade 3 Pain (3rd) [N=212,217,144,125,138,150]	11	7	0	0
Any Pain (4th) [N=206,211,139,120,136,152]	79	77	19	106
Grade 3 Pain (4th) [N=206,211,139,120,136,152]	1	0	0	10
Any Pain (5th) [N=206,206,140,121,132,147]	83	80	58	48
Grade 3 Pain (5th) [N=206,206,140,121,132,147]	0	1	1	0
Any Erythema (1st) [N=227,231,154,134,151,159]	23	24	18	12
Grade 3 Erythema (1st)[N=227,231,154,134,151,159]	0	3	1	0
Any Erythema (2nd) [N=214,216,150,128,144,151]	3	5	9	1
Grade3Erythema(2nd)[N=214,216,150,128,144,151]	0	0	2	0
Any Erythema (3rd) [N=212,217,144,125,138,150]	33	29	0	2
Grade 3 Erythema (3rd)[N=212,217,144,125,138,150]	2	6	0	0
Any Erythema (4th) [N=206,211,139,120,136,152]	1	1	0	12
Grade 3 Erythema(4th) [N=206,211,139,120,136,152]	0	0	0	1
Any Erythema (5th) [N=206,206,140,121,132,147]	1	1	1	0
Grade 3 Erythema(5th) [N=206,206,140,121,132,147]	0	0	0	0
Any Induration (1st) [N=227,231,154,134,151,159]	24	23	14	13
Grade 3 Induration(1st)[N=227,231,154,134,15	0	0	0	1
Any Induration(2nd) [N=214,216,150,128,144,151]	2	2	12	0

Grade3 Induration(2nd)[N=214,216,150,128,14	0	0	0	0
Any Induration (3rd) [N=212,217,144,125,138,150]	27	18	1	0
Grade3 Induration(3rd)[N=212,217,144,125,13	2	1	0	0
Any Induration(4th) [N=206,211,139,120,136,152]	2	3	0	10
Grade3 Induration(4th)[N=206,211,139,120,13	0	0	0	1
Any Induration (5th) [N=206,206,140,121,132,147]	2	3	1	2
Grade3 Induration(5th)[N=206,206,140,121,13	0	0	0	1
Any Fatigue (1st) [N=227,231,154,134,151,159]	126	121	84	68
Grade3 Fatigue(1st) [N=227,231,154,134,151,159]	7	7	4	3
Any Fatigue (2nd) [N=214,216,150,128,144,151]	61	64	64	40
Grade 3 Fatigue(2nd) [N=214,216,150,128,144,151]	0	3	4	2
Any Fatigue (3rd) [N=212,217,144,125,138,150]	106	96	44	32
Grade 3 Fatigue(3rd) [N=212,217,144,125,138,150]	4	5	1	0
Any Fatigue (4th) [N=206,211,139,120,136,152]	50	56	37	51
Grade 3 Fatigue(4th) [N=206,211,139,120,136,152]	2	3	0	5
Any Fatigue (5th) [N=206,206,140,121,132,147]	62	59	37	41
Grade 3 Fatigue(5th) [N=206,206,140,121,132,147]	1	2	4	0
Any Headache (1st) [N=227,231,154,134,151,159]	103	92	65	52
Grade 3 Headache(1st) [N=227,231,154,134,151,159]	4	3	5	2
Any Headache (2nd) [N=214,216,150,128,144,151]	67	47	70	36
Grade 3 Headache(2nd) [N=214,216,150,128,144,151]	1	2	3	2
Any Headache (3rd) [N=212,217,144,125,138,150]	90	76	42	28
Grade 3 Headache(3rd) [N=212,217,144,125,138,150]	3	4	1	0
Any Headache (4th) [N=206,211,139,120,136,152]	49	35	26	44
Grade 3 Headache(4th) [N=206,211,139,120,136,152]	3	3	0	2
Any Headache (5th) [N=206,206,140,121,132,147]	64	40	33	33
Grade 3 Headache(5th) [N=206,206,140,121,132,147]	1	1	2	1
Any Myalgia (1st) [N=227,231,154,134,151,159]	62	53	39	34
Grade 3 Myalgia (1st)[N=227,231,154,134,151,159]	2	4	2	2
Any Myalgia (2nd) [N=214,216,150,128,144,151]	15	20	27	15
Grade 3 Myalgia(2nd) [N=214,216,150,128,144,151]	0	3	1	1

Any Myalgia (3rd) [N=212,217,144,125,138,150]	52	40	13	10
Grade 3 Myalgia (3rd) [N=212,217,144,125,138,150]	2	2	0	0
Any Myalgia (4th) [N=206,211,139,120,136,152]	17	20	11	26
Grade 3 Myalgia(4th) [N=206,211,139,120,136,152]	1	1	1	2
Any Myalgia (5th) [N=206,206,140,121,132,147]	16	26	19	12
Grade 3 Myalgia (5th) [N=206,206,140,121,132,147]	0	1	0	0
Any Appetite Loss(1st)[N=227,231,154,134,151,159]	41	33	28	22
Grade3AppetiteLoss(1st)[N=227,231,154,134,151,159	2	3	0	0
AnyAppetiteLoss(2nd)[N=214,216,150,128,144,151]	17	11	15	12
Grade3AppetiteLoss(2nd)[N=214,216,150,128,144,151	0	1	0	0
AnyAppetiteLoss(3rd)[N=212,217,144,125,138,150]	28	28	7	7
Grade3AppetiteLoss(3rd)[N=212,217,144,125,138,150	1	0	1	0
Any Appetite Loss(4th)[N=206,211,139,120,136,152]	11	10	4	13
Grade3AppetiteLoss(4th)[N=206,211,139,120,136,152	0	0	0	0
Any Appetite Loss(5th)[N=206,206,140,121,132,147]	18	14	9	9
Grade3AppetiteLoss(5th)[N=206,206,140,121,132,147	0	0	1	0
Any Nausea (1st) [N=227,231,154,134,151,159]	42	36	28	17
Grade 3 Nausea (1st) [N=227,231,154,134,151,159]	1	0	0	0
Any Nausea (2nd) [N=214,216,150,128,144,151]	17	15	20	10
Grade 3 Nausea (2nd) [N=214,216,150,128,144,151]	0	0	0	0
Any Nausea (3rd) [N=212,217,144,125,138,150]	35	24	10	8
Grade 3 Nausea (3rd) [N=212,217,144,125,138,150]	0	0	0	0
Any Nausea (4th) [N=206,211,139,120,136,152]	21	13	9	11
Grade 3 Nausea (4th) [N=206,211,139,120,136,152]	1	0	0	0
Any Nausea (5th) [N=206,206,140,121,132,147]	16	15	8	11
Grade 3 Nausea(5th) [N=206,206,140,121,132,147]	0	0	0	0
Any Chills (1st) [N=227,231,154,134,151,159]	45	36	41	24
Grade 3 Chills (1st) [N=227,231,154,134,151,159]	1	0	1	1
Any Chills (2nd) [N=214,216,150,128,144,151]	17	26	26	12
Grade 3 Chills (2nd) [N=214,216,150,128,144,151]	0	1	1	0
Any Chills(3rd) [N=212,217,144,125,138,150]	33	33	9	7

Grade 3 Chills(3rd) [N=212,217,144,125,138,150]	1	1	0	0
Any Chills (4th) [N=206,211,139,120,136,152]	11	11	10	12
Grade 3 Chills (4th) [N=206,211,139,120,136,152]	2	0	0	0
Any Chills (5th) [N=206,206,140,121,132,147]	19	23	17	11
Grade 3 Chills(5th) [N=206,206,140,121,132,147]	0	0	0	1
Fever (1st) [N=227,231,154,133,151,158]	5	4	5	1
Fever (2nd) [N=214,216,149,127,144,151]	2	6	4	2
Fever (3rd) [N=212,217,143,124,138,150]	6	3	2	0
Fever (4th) [N=206,211,138,119,136,151]	0	2	0	3
Fever (5th) [N=206,206,139,120,132,147]	5	1	2	0
Pain/Fever prevention(1)N=227,231,154,134,151,1	28	34	21	26
Pain/Fever prevention(2)N=214,216,150,128,144,1	5	7	18	5
Pain/Fever prevention(3)N=212,217,144,125,138,1	32	34	3	2
Pain/Fever prevention(4)N=206,211,139,120,136,1	6	5	3	19
Pain/Fever prevention(5)N=206,206,140,121,132,1	5	9	4	1
Pain/Fever treatment(1)N=227,231,154,134,151,1	31	45	27	32
Pain/Fever treatment(2)N=214,216,150,128,144,1	3	4	20	3
Pain/Fever treatment(3)N=212,217,144,125,138,1	38	37	2	4
Pain/Fever treatment(4)N=206,211,139,120,136,1	7	4	2	22
Pain/Fever treatment(5)N=206,206,140,121,132,1	3	8	2	3
Any Arthralgia (1st) [N=227,231,154,134,151,159]	25	14	13	17
Grade3Arthralgia(1st) [N=227,231,154,134,151,159]	0	1	0	0
Any Arthralgia (2nd) [N=214,216,150,128,144,151]	7	11	10	9
Grade3Arthralgia(2nd)[N=214,216,150, 128,144,151]	0	0	0	1
Any Arthralgia (3rd) [N=212,217,144,125,138,150]	16	17	4	3
Grade3Arthralgia(3rd)[N=212,217,144, 125,138,150]	0	1	0	0
Any Arthralgia (4th) [N=206,211,139,120,136,152]	8	10	5	10
Grade3Arthralgia(4th)[N=206,211,139, 120,136,152]	1	0	0	0
Any Arthralgia(5th)[N=206,206,140,121,132	8	9	8	6
Grade3Arthralgia(5th)[N=206,206,140, 121,132,147]	0	0	0	0

End point values	ABCWY_0_11 Group	ABCWY_0_2_6 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	151	159		
Units: Subjects				
Any AE [N= 228, 231, 155, 134, 151, 159]	151	157		
Any Local AE [N= 228, 231, 155, 134, 151, 159]	147	156		
Any Systemic AE [N= 228, 231, 155, 134, 151, 159]	134	143		
Any Pain (1st) [N=227,231,154,134,151,159]	80	146		
Grade 3 Pain (1st) [N=227,231,154,134,151,159]	0	6		
Any Pain (2nd) [N=214,216,150,128,144,151]	135	51		
Grade 3 Pain (2nd) [N=214,216,150,128,144,151]	11	0		
Any Pain (3rd) [N=212,217,144,125,138,150]	16	133		
Grade 3 Pain (3rd) [N=212,217,144,125,138,150]	0	5		
Any Pain (4th) [N=206,211,139,120,136,152]	44	138		
Grade 3 Pain (4th) [N=206,211,139,120,136,152]	0	9		
Any Pain (5th) [N=206,206,140,121,132,147]	119	64		
Grade 3 Pain (5th) [N=206,206,140,121,132,147]	11	1		
Any Erythema (1st) [N=227,231,154,134,151,159]	1	23		
Grade 3 Erythema (1st)[N=227,231,154,134,151,159]	0	2		
Any Erythema (2nd) [N=214,216,150,128,144,151]	17	3		
Grade3Erythema(2nd)[N=214,216,150, 128,144,151]	4	1		
Any Erythema (3rd) [N=212,217,144,125,138,150]	0	20		
Grade 3 Erythema (3rd)[N=212,217,144,125,138,150]	0	1		
Any Erythema (4th) [N=206,211,139,120,136,152]	0	16		
Grade 3 Erythema(4th) [N=206,211,139,120,136,152]	0	5		
Any Erythema (5th) [N=206,206,140,121,132,147]	11	0		
Grade 3 Erythema(5th) [N=206,206,140,121,132,147]	1	0		
Any Induration (1st) [N=227,231,154,134,151,159]	3	21		
Grade 3 Induration(1st)[N=227,231,154,134,15	0	1		
Any Induration(2nd) [N=214,216,150,128,144,151]	12	2		

Grade3 Induration(2nd)[N=214,216,150,128,14	0	0		
Any Induration (3rd) [N=212,217,144,125,138,150]	1	22		
Grade3 Induration(3rd)[N=212,217,144,125,13	0	0		
Any Induration(4th) [N=206,211,139,120,136,152]	0	14		
Grade3 Induration(4th)[N=206,211,139,120,13	0	1		
Any Induration (5th) [N=206,206,140,121,132,147]	16	1		
Grade3 Induration(5th)[N=206,206,140,121,13	1	0		
Any Fatigue (1st) [N=227,231,154,134,151,159]	68	76		
Grade3 Fatigue(1st) [N=227,231,154,134,151,159]	3	4		
Any Fatigue (2nd) [N=214,216,150,128,144,151]	64	49		
Grade 3 Fatigue(2nd) [N=214,216,150,128,144,151]	1	0		
Any Fatigue (3rd) [N=212,217,144,125,138,150]	32	55		
Grade 3 Fatigue(3rd) [N=212,217,144,125,138,150]	1	1		
Any Fatigue (4th) [N=206,211,139,120,136,152]	35	73		
Grade 3 Fatigue(4th) [N=206,211,139,120,136,152]	2	3		
Any Fatigue (5th) [N=206,206,140,121,132,147]	51	46		
Grade 3 Fatigue(5th) [N=206,206,140,121,132,147]	6	3		
Any Headache (1st) [N=227,231,154,134,151,159]	63	64		
Grade 3 Headache(1st) [N=227,231,154,134,151,159]	2	3		
Any Headache (2nd) [N=214,216,150,128,144,151]	63	41		
Grade 3 Headache(2nd) [N=214,216,150,128,144,151]	4	2		
Any Headache (3rd) [N=212,217,144,125,138,150]	30	53		
Grade 3 Headache(3rd) [N=212,217,144,125,138,150]	3	0		
Any Headache (4th) [N=206,211,139,120,136,152]	26	52		
Grade 3 Headache(4th) [N=206,211,139,120,136,152]	0	4		
Any Headache (5th) [N=206,206,140,121,132,147]	52	37		
Grade 3 Headache(5th) [N=206,206,140,121,132,147]	2	2		
Any Myalgia (1st) [N=227,231,154,134,151,159]	33	40		
Grade 3 Myalgia (1st)[N=227,231,154,134,151,159]	0	3		
Any Myalgia (2nd) [N=214,216,150,128,144,151]	37	18		
Grade 3 Myalgia(2nd) [N=214,216,150,128,144,151]	1	0		

Any Myalgia (3rd) [N=212,217,144,125,138,150]	13	34		
Grade 3 Myalgia (3rd) [N=212,217,144,125,138,150]	2	2		
Any Myalgia (4th) [N=206,211,139,120,136,152]	13	39		
Grade 3 Myalgia(4th) [N=206,211,139,120,136,152]	0	2		
Any Myalgia (5th) [N=206,206,140,121,132,147]	21	19		
Grade 3 Myalgia (5th) [N=206,206,140,121,132,147]	1	1		
Any Appetite Loss(1st)[N=227,231,154,134,151,159]	14	18		
Grade3AppetiteLoss(1st)[N=227,231,154,134,151,159	0	0		
AnyAppetiteLoss(2nd)[N=214,216,150,128,144,151]	19	9		
Grade3AppetiteLoss(2nd)[N=214,216,150,128,144,151	2	0		
AnyAppetiteLoss(3rd)[N=212,217,144,125,138,150]	11	17		
Grade3AppetiteLoss(3rd)[N=212,217,144,125,138,150	1	0		
Any Appetite Loss(4th)[N=206,211,139,120,136,152]	11	23		
Grade3AppetiteLoss(4th)[N=206,211,139,120,136,152	0	0		
Any Appetite Loss(5th)[N=206,206,140,121,132,147]	22	7		
Grade3AppetiteLoss(5th)[N=206,206,140,121,132,147	0	0		
Any Nausea (1st) [N=227,231,154,134,151,159]	26	21		
Grade 3 Nausea (1st) [N=227,231,154,134,151,159]	0	1		
Any Nausea (2nd) [N=214,216,150,128,144,151]	26	15		
Grade 3 Nausea (2nd) [N=214,216,150,128,144,151]	0	0		
Any Nausea (3rd) [N=212,217,144,125,138,150]	4	21		
Grade 3 Nausea (3rd) [N=212,217,144,125,138,150]	0	0		
Any Nausea (4th) [N=206,211,139,120,136,152]	14	23		
Grade 3 Nausea (4th) [N=206,211,139,120,136,152]	0	0		
Any Nausea (5th) [N=206,206,140,121,132,147]	21	12		
Grade 3 Nausea(5th) [N=206,206,140,121,132,147]	0	0		
Any Chills (1st) [N=227,231,154,134,151,159]	27	40		
Grade 3 Chills (1st) [N=227,231,154,134,151,159]	2	1		
Any Chills (2nd) [N=214,216,150,128,144,151]	32	15		
Grade 3 Chills (2nd) [N=214,216,150,128,144,151]	0	0		
Any Chills(3rd) [N=212,217,144,125,138,150]	12	22		

Grade 3 Chills(3rd) [N=212,217,144,125,138,150]	1	0		
Any Chills (4th) [N=206,211,139,120,136,152]	9	31		
Grade 3 Chills (4th) [N=206,211,139,120,136,152]	0	1		
Any Chills (5th) [N=206,206,140,121,132,147]	22	13		
Grade 3 Chills(5th) [N=206,206,140,121,132,147]	0	0		
Fever (1st) [N=227,231,154,133,151,158]	2	3		
Fever (2nd) [N=214,216,149,127,144,151]	9	3		
Fever (3rd) [N=212,217,143,124,138,150]	4	4		
Fever (4th) [N=206,211,138,119,136,151]	0	7		
Fever (5th) [N=206,206,139,120,132,147]	3	1		
Pain/Fever prevention(1)N=227,231,154,134,151,1	5	34		
Pain/Fever prevention(2)N=214,216,150,128,144,1	24	7		
Pain/Fever prevention(3)N=212,217,144,125,138,1	3	21		
Pain/Fever prevention(4)N=206,211,139,120,136,1	3	25		
Pain/Fever prevention(5)N=206,206,140,121,132,1	26	3		
Pain/Fever treatment(1)N=227,231,154,134,151,1	6	31		
Pain/Fever treatment(2)N=214,216,150,128,144,1	29	4		
Pain/Fever treatment(3)N=212,217,144,125,138,1	2	23		
Pain/Fever treatment(4)N=206,211,139,120,136,1	2	27		
Pain/Fever treatment(5)N=206,206,140,121,132,1	29	2		
Any Arthralgia (1st) [N=227,231,154,134,151,159]	12	14		
Grade3Arthralgia(1st) [N=227,231,154,134,151,159]	1	2		
Any Arthralgia (2nd) [N=214,216,150,128,144,151]	8	7		
Grade3Arthralgia(2nd)[N=214,216,150,128,144,151]	0	1		
Any Arthralgia (3rd) [N=212,217,144,125,138,150]	6	11		
Grade3Arthralgia(3rd)[N=212,217,144,125,138,150]	0	0		
Any Arthralgia (4th) [N=206,211,139,120,136,152]	7	18		
Grade3Arthralgia(4th)[N=206,211,139,120,136,152]	0	2		
Any Arthralgia(5th)[N=206,206,140,121,132	11	11		
Grade3Arthralgia(5th)[N=206,206,140,121,132,147]	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting unsolicited AEs after any vaccination

End point title	Number of subjects reporting unsolicited AEs after any vaccination

End point description:

The number of subjects reporting unsolicited AEs and possibly or probably related unsolicited AEs 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. Possibly or probably related AE = AE assessed by the investigator as related to the vaccination.
The analysis was performed on the Unsolicited Safety Set population, which included all subjects who received a study vaccination and who had post-vaccination unsolicited adverse event records.

End point type	Secondary

End point timeframe:

From Day 1 through Day 30 after any vaccination

End point values	rMenB_0_2 Group	ABCWY_ 0_2 Group	ABCWY_0_1 Group	ABCWY_0_6 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	221	228	151	129
Units: Subjects				
Any AE(s)	146	148	93	76
Possibly or Probably Related AE(s)	25	31	23	16

End point values	ABCWY_0_11 Group	ABCWY_0_2_6 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	147	157		
Units: Subjects				
Any AE(s)	97	104		
Possibly or Probably Related AE(s)	18	27		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any serious adverse events (SAEs) and other significant AE(s)

End point title	Number of subjects reporting any serious adverse events (SAEs) and other significant AE(s)

End point description:

The number of subjects reporting any SAE, possibly or probably related SAE(s), medically attended AE(s) (MAEs), AE(s) leading to premature withdrawal,AE(s) leading to death,AE(s) leading to hospitalization and AE(s) leading to dose reduction, interruption and delay in study vaccination 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.Possibly or probably related SAE=SAE assessed by the investigator as related to the vaccination.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 for any reason. The analysis was performed on the Unsolicited Safety Set population, which included all subjects who received a study vaccination and who had post-vaccination unsolicited AE records.

End point type	Secondary

End point timeframe:

During the entire study period (from Month 0 up to Month 13)

End point values	rMenB_0_2 Group	ABCWY_ 0_2 Group	ABCWY_0_1 Group	ABCWY_0_6 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	221	228	151	129
Units: Subjects				
Any SAE(s)	9	3	8	7
Possibly or Probably Related SAE(s)	0	1	1	0
Medically Attended AE(s)	103	97	68	57
AE(s) leading to premature withdrawal	2	6	4	2
AE(s) leading to Death	0	0	0	0
AE(s) leading to Hospitalization	9	1	7	6
AE(s)leadingtodosereduction,interruption,vaccdelay	8	8	7	2

End point values	ABCWY_0_11 Group	ABCWY_0_2_6 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	147	157		
Units: Subjects				
Any SAE(s)	2	6		
Possibly or Probably Related SAE(s)	0	0		
Medically Attended AE(s)	67	79		
AE(s) leading to premature withdrawal	1	3		
AE(s) leading to Death	0	0		
AE(s) leading to Hospitalization	1	6		
AE(s)leadingtodosereduction,interruption,vaccdelay	4	5		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited AEs were collected from Day 1 (6 hours) to Day 7; Unsolicited AEs were collected from Day 1 to Day 30; SAEs, AEs leading to withdrawal and medically attended AEs were collected throughout the entire study period (from Month 0 up to Month 13).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups

Reporting group title	rMenB_0_2 Group

Reporting group description:

Subjects received two injections of Bexsero™ vaccine at Visit Month 0 and Visit Month 2, Havrix® vaccine at Visit Month 6 and Visit Month 12 and saline placebo at Visit Month 1.

Reporting group title	ABCWY_ 0_2 Group

Reporting group description:

Subjects received MenABCWY vaccine at Visit Month 0 and Visit Month 2, Havrix® vaccine at Visit Month 6 and Visit Month 12 and saline placebo at Visit Month 1.

Reporting group title	ABCWY_0_1 Group

Reporting group description:

Subjects received MenABCWY vaccine at Visit Month 0 and Visit Month 1, Havrix® vaccine at Visit Month 2 and Visit Month 12 and saline placebo at Visit Month 6.

Reporting group title	ABCWY_0_6 Group

Reporting group description:

Subjects received MenABCWY vaccine at Visit Month 0 and Visit Month 6, Havrix® vaccine at Visit Month 1 and Visit Month 12 and saline placebo at Visit Month 2.

Reporting group title	ABCWY_0_11 Group

Reporting group description:

Subjects received MenABCWY vaccine at Visit Month 1 and Visit Month 12, Havrix® vaccine at Visit Month 0 and Visit Month 6 and saline placebo at Visit Month 2.

Reporting group title	ABCWY_0_2_6 Group

Reporting group description:

Subjects received MenABCWY vaccine at Visit Month 0, Visit Month 2 and Visit Month 6 and Havrix® vaccine at Visit Month 1 and Visit Month 12.

Serious adverse events	rMenB_0_2 Group	ABCWY_ 0_2 Group	ABCWY_0_1 Group
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 228 (3.95%)	3 / 231 (1.30%)	8 / 155 (5.16%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Fibroadenoma of breast			

subjects affected / exposed[1]	0 / 221 (0.00%)	0 / 228 (0.00%)	1 / 151 (0.66%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Tooth extraction			
subjects affected / exposed[2]	0 / 221 (0.00%)	0 / 228 (0.00%)	0 / 151 (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
Pregnancy, puerperium and perinatal conditions			
Abortion incomplete			
subjects affected / exposed[3]	1 / 221 (0.45%)	0 / 228 (0.00%)	0 / 151 (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
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed[4]	1 / 221 (0.45%)	0 / 228 (0.00%)	0 / 151 (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
Fatigue			
subjects affected / exposed[5]	0 / 221 (0.00%)	0 / 228 (0.00%)	0 / 151 (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			
Testicular torsion			
subjects affected / exposed[6]	0 / 221 (0.00%)	0 / 228 (0.00%)	0 / 151 (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			
Depression			
subjects affected / exposed[7]	1 / 221 (0.45%)	0 / 228 (0.00%)	0 / 151 (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
Mental disorder			

subjects affected / exposed[8]	0 / 221 (0.00%)	0 / 228 (0.00%)	0 / 151 (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
Suicidal ideation			
subjects affected / exposed[9]	0 / 221 (0.00%)	1 / 228 (0.44%)	1 / 151 (0.66%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Carbon monoxide poisoning			
subjects affected / exposed[10]	0 / 221 (0.00%)	1 / 228 (0.44%)	0 / 151 (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
Femur fracture			
subjects affected / exposed[11]	0 / 221 (0.00%)	0 / 228 (0.00%)	0 / 151 (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
Forearm fracture			
subjects affected / exposed[12]	1 / 221 (0.45%)	0 / 228 (0.00%)	0 / 151 (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
Lower limb fracture			
subjects affected / exposed[13]	0 / 221 (0.00%)	0 / 228 (0.00%)	0 / 151 (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
Cardiac disorders			
Atrioventricular block second degree			
subjects affected / exposed[14]	1 / 221 (0.45%)	0 / 228 (0.00%)	0 / 151 (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
Nervous system disorders			
Partial seizures			
subjects affected / exposed[15]	0 / 221 (0.00%)	0 / 228 (0.00%)	0 / 151 (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

Seizure			
subjects affected / exposed[16]	0 / 221 (0.00%)	1 / 228 (0.44%)	0 / 151 (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
Syncope			
subjects affected / exposed[17]	0 / 221 (0.00%)	0 / 228 (0.00%)	0 / 151 (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
Blood and lymphatic system disorders			
Iron deficiency anaemia			
subjects affected / exposed[18]	2 / 221 (0.90%)	0 / 228 (0.00%)	0 / 151 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal migraine			
subjects affected / exposed[19]	1 / 221 (0.45%)	0 / 228 (0.00%)	0 / 151 (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
Abdominal pain			
subjects affected / exposed[20]	0 / 221 (0.00%)	0 / 228 (0.00%)	1 / 151 (0.66%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper			
subjects affected / exposed[21]	1 / 221 (0.45%)	0 / 228 (0.00%)	0 / 151 (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
Crohn's disease			
subjects affected / exposed[22]	0 / 221 (0.00%)	0 / 228 (0.00%)	0 / 151 (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
Renal and urinary disorders			
Tubulointerstitial nephritis			

subjects affected / exposed[23]	1 / 221 (0.45%)	0 / 228 (0.00%)	0 / 151 (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
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed[24]	0 / 221 (0.00%)	0 / 228 (0.00%)	0 / 151 (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
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed[25]	0 / 221 (0.00%)	0 / 228 (0.00%)	1 / 151 (0.66%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Connective tissue disorder			
subjects affected / exposed[26]	0 / 221 (0.00%)	0 / 228 (0.00%)	1 / 151 (0.66%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Torticollis			
subjects affected / exposed[27]	0 / 221 (0.00%)	0 / 228 (0.00%)	0 / 151 (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
Infections and infestations			
Appendicitis			
subjects affected / exposed[28]	1 / 221 (0.45%)	0 / 228 (0.00%)	2 / 151 (1.32%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia urinary tract infection			
subjects affected / exposed[29]	1 / 221 (0.45%)	0 / 228 (0.00%)	0 / 151 (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
Gastroenteritis			
subjects affected / exposed[30]	0 / 221 (0.00%)	0 / 228 (0.00%)	0 / 151 (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

Infectious mononucleosis			
subjects affected / exposed[31]	1 / 221 (0.45%)	0 / 228 (0.00%)	0 / 151 (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
Nasopharyngitis			
subjects affected / exposed[32]	1 / 221 (0.45%)	0 / 228 (0.00%)	0 / 151 (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
Pelvic inflammatory disease			
subjects affected / exposed[33]	1 / 221 (0.45%)	0 / 228 (0.00%)	0 / 151 (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
Peritonsillar abscess			
subjects affected / exposed[34]	0 / 221 (0.00%)	0 / 228 (0.00%)	1 / 151 (0.66%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillitis			
subjects affected / exposed[35]	0 / 221 (0.00%)	0 / 228 (0.00%)	0 / 151 (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
Urinary tract infection			
subjects affected / exposed[36]	1 / 221 (0.45%)	0 / 228 (0.00%)	0 / 151 (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
Metabolism and nutrition disorders			
Failure to thrive			
subjects affected / exposed[37]	0 / 221 (0.00%)	0 / 228 (0.00%)	1 / 151 (0.66%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Obesity			
subjects affected / exposed[38]	0 / 221 (0.00%)	0 / 228 (0.00%)	0 / 151 (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
Type 1 diabetes mellitus			

subjects affected / exposed[39]	0 / 221 (0.00%)	0 / 228 (0.00%)	0 / 151 (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

Serious adverse events	ABCWY_0_6 Group	ABCWY_0_11 Group	ABCWY_0_2_6 Group
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 134 (5.22%)	2 / 151 (1.32%)	6 / 159 (3.77%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Fibroadenoma of breast			
subjects affected / exposed[1]	0 / 129 (0.00%)	0 / 147 (0.00%)	0 / 157 (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
Surgical and medical procedures			
Tooth extraction			
subjects affected / exposed[2]	1 / 129 (0.78%)	0 / 147 (0.00%)	0 / 157 (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
Pregnancy, puerperium and perinatal conditions			
Abortion incomplete			
subjects affected / exposed[3]	0 / 129 (0.00%)	0 / 147 (0.00%)	0 / 157 (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
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed[4]	0 / 129 (0.00%)	0 / 147 (0.00%)	0 / 157 (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
Fatigue			
subjects affected / exposed[5]	1 / 129 (0.78%)	0 / 147 (0.00%)	0 / 157 (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
Reproductive system and breast disorders			

Testicular torsion			
subjects affected / exposed[6]	0 / 129 (0.00%)	0 / 147 (0.00%)	1 / 157 (0.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Depression			
subjects affected / exposed[7]	0 / 129 (0.00%)	0 / 147 (0.00%)	0 / 157 (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
Mental disorder			
subjects affected / exposed[8]	1 / 129 (0.78%)	0 / 147 (0.00%)	0 / 157 (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
Suicidal ideation			
subjects affected / exposed[9]	0 / 129 (0.00%)	0 / 147 (0.00%)	0 / 157 (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
Injury, poisoning and procedural complications			
Carbon monoxide poisoning			
subjects affected / exposed[10]	0 / 129 (0.00%)	0 / 147 (0.00%)	0 / 157 (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
Femur fracture			
subjects affected / exposed[11]	0 / 129 (0.00%)	0 / 147 (0.00%)	1 / 157 (0.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Forearm fracture			
subjects affected / exposed[12]	0 / 129 (0.00%)	0 / 147 (0.00%)	0 / 157 (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
Lower limb fracture			
subjects affected / exposed[13]	0 / 129 (0.00%)	0 / 147 (0.00%)	1 / 157 (0.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Cardiac disorders			
Atrioventricular block second degree			
subjects affected / exposed[14]	0 / 129 (0.00%)	0 / 147 (0.00%)	0 / 157 (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
Nervous system disorders			
Partial seizures			
subjects affected / exposed[15]	0 / 129 (0.00%)	1 / 147 (0.68%)	0 / 157 (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
Seizure			
subjects affected / exposed[16]	0 / 129 (0.00%)	0 / 147 (0.00%)	0 / 157 (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
Syncope			
subjects affected / exposed[17]	0 / 129 (0.00%)	1 / 147 (0.68%)	0 / 157 (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
Blood and lymphatic system disorders			
Iron deficiency anaemia			
subjects affected / exposed[18]	0 / 129 (0.00%)	0 / 147 (0.00%)	0 / 157 (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
Gastrointestinal disorders			
Abdominal migraine			
subjects affected / exposed[19]	0 / 129 (0.00%)	0 / 147 (0.00%)	0 / 157 (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
Abdominal pain			
subjects affected / exposed[20]	1 / 129 (0.78%)	0 / 147 (0.00%)	0 / 157 (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
Abdominal pain upper			

subjects affected / exposed[21]	0 / 129 (0.00%)	0 / 147 (0.00%)	0 / 157 (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
Crohn's disease			
subjects affected / exposed[22]	1 / 129 (0.78%)	0 / 147 (0.00%)	0 / 157 (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
Renal and urinary disorders			
Tubulointerstitial nephritis			
subjects affected / exposed[23]	0 / 129 (0.00%)	0 / 147 (0.00%)	0 / 157 (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
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed[24]	0 / 129 (0.00%)	0 / 147 (0.00%)	1 / 157 (0.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed[25]	0 / 129 (0.00%)	0 / 147 (0.00%)	0 / 157 (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
Connective tissue disorder			
subjects affected / exposed[26]	0 / 129 (0.00%)	0 / 147 (0.00%)	0 / 157 (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
Torticollis			
subjects affected / exposed[27]	0 / 129 (0.00%)	0 / 147 (0.00%)	1 / 157 (0.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			

subjects affected / exposed[28]	0 / 129 (0.00%)	0 / 147 (0.00%)	0 / 157 (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
Escherichia urinary tract infection			
subjects affected / exposed[29]	0 / 129 (0.00%)	0 / 147 (0.00%)	0 / 157 (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
Gastroenteritis			
subjects affected / exposed[30]	1 / 129 (0.78%)	0 / 147 (0.00%)	0 / 157 (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
Infectious mononucleosis			
subjects affected / exposed[31]	0 / 129 (0.00%)	0 / 147 (0.00%)	0 / 157 (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
Nasopharyngitis			
subjects affected / exposed[32]	0 / 129 (0.00%)	0 / 147 (0.00%)	0 / 157 (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
Pelvic inflammatory disease			
subjects affected / exposed[33]	0 / 129 (0.00%)	0 / 147 (0.00%)	1 / 157 (0.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonsillar abscess			
subjects affected / exposed[34]	0 / 129 (0.00%)	0 / 147 (0.00%)	0 / 157 (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
Tonsillitis			
subjects affected / exposed[35]	1 / 129 (0.78%)	0 / 147 (0.00%)	0 / 157 (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[36]	0 / 129 (0.00%)	0 / 147 (0.00%)	0 / 157 (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
Metabolism and nutrition disorders			
Failure to thrive			
subjects affected / exposed[37]	0 / 129 (0.00%)	0 / 147 (0.00%)	0 / 157 (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
Obesity			
subjects affected / exposed[38]	0 / 129 (0.00%)	0 / 147 (0.00%)	1 / 157 (0.64%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Type 1 diabetes mellitus			
subjects affected / exposed[39]	1 / 129 (0.78%)	0 / 147 (0.00%)	0 / 157 (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

Notes:

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

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

Non-serious adverse events	rMenB_0_2 Group	ABCWY_ 0_2 Group	ABCWY_0_1 Group
Total subjects affected by non-serious adverse events subjects affected / exposed	226 / 228 (99.12%)	229 / 231 (99.13%)	153 / 155 (98.71%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Arthralgia			
subjects affected / exposed	48 / 228 (21.05%)	48 / 231 (20.78%)	28 / 155 (18.06%)
occurrences (all)	109	125	57
Injury, poisoning and procedural complications			
Respiratory tract infection			
subjects affected / exposed	15 / 228 (6.58%)	12 / 231 (5.19%)	10 / 155 (6.45%)
occurrences (all)	24	15	16
Nervous system disorders			
Headache			
subjects affected / exposed	165 / 228 (72.37%)	149 / 231 (64.50%)	114 / 155 (73.55%)
occurrences (all)	830	593	496
General disorders and administration site conditions			
Chills			
subjects affected / exposed	80 / 228 (35.09%)	76 / 231 (32.90%)	61 / 155 (39.35%)
occurrences (all)	236	216	172
Fatigue			
subjects affected / exposed	169 / 228 (74.12%)	165 / 231 (71.43%)	119 / 155 (76.77%)
occurrences (all)	956	891	534
Injection site erythema			
subjects affected / exposed	131 / 228 (57.46%)	131 / 231 (56.71%)	80 / 155 (51.61%)
occurrences (all)	465	367	271
Injection site induration			
subjects affected / exposed	110 / 228 (48.25%)	98 / 231 (42.42%)	67 / 155 (43.23%)
occurrences (all)	437	359	260
Injection site pain			
subjects affected / exposed	221 / 228 (96.93%)	225 / 231 (97.40%)	148 / 155 (95.48%)
occurrences (all)	1870	1598	1003
Pyrexia			
subjects affected / exposed	27 / 228 (11.84%)	27 / 231 (11.69%)	20 / 155 (12.90%)
occurrences (all)	37	34	26
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	16 / 228 (7.02%)	9 / 231 (3.90%)	6 / 155 (3.87%)
occurrences (all)	22	9	6
Nausea			

subjects affected / exposed	74 / 228 (32.46%)	68 / 231 (29.44%)	51 / 155 (32.90%)
occurrences (all)	232	145	136
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	12 / 228 (5.26%)	5 / 231 (2.16%)	6 / 155 (3.87%)
occurrences (all)	14	6	7
Oropharyngeal pain			
subjects affected / exposed	12 / 228 (5.26%)	13 / 231 (5.63%)	9 / 155 (5.81%)
occurrences (all)	14	13	13
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	103 / 228 (45.18%)	99 / 231 (42.86%)	69 / 155 (44.52%)
occurrences (all)	271	315	169
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	15 / 228 (6.58%)	11 / 231 (4.76%)	13 / 155 (8.39%)
occurrences (all)	16	11	13
Nasopharyngitis			
subjects affected / exposed	37 / 228 (16.23%)	30 / 231 (12.99%)	28 / 155 (18.06%)
occurrences (all)	53	50	40
Pharyngitis			
subjects affected / exposed	16 / 228 (7.02%)	21 / 231 (9.09%)	7 / 155 (4.52%)
occurrences (all)	16	21	9
Rhinitis			
subjects affected / exposed	15 / 228 (6.58%)	18 / 231 (7.79%)	7 / 155 (4.52%)
occurrences (all)	18	21	10
Tonsillitis			
subjects affected / exposed	7 / 228 (3.07%)	10 / 231 (4.33%)	3 / 155 (1.94%)
occurrences (all)	9	11	4
Upper respiratory tract infection			
subjects affected / exposed	53 / 228 (23.25%)	58 / 231 (25.11%)	37 / 155 (23.87%)
occurrences (all)	74	92	52
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	69 / 228 (30.26%)	64 / 231 (27.71%)	45 / 155 (29.03%)
occurrences (all)	208	164	107

Non-serious adverse events	ABCWY_0_6 Group	ABCWY_0_11 Group	ABCWY_0_2_6 Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	131 / 134 (97.76%)	151 / 151 (100.00%)	158 / 159 (99.37%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Arthralgia			
subjects affected / exposed	31 / 134 (23.13%)	27 / 151 (17.88%)	38 / 159 (23.90%)
occurrences (all)	96	68	101
Injury, poisoning and procedural complications			
Respiratory tract infection			
subjects affected / exposed	5 / 134 (3.73%)	6 / 151 (3.97%)	10 / 159 (6.29%)
occurrences (all)	12	12	13
Nervous system disorders			
Headache			
subjects affected / exposed	93 / 134 (69.40%)	110 / 151 (72.85%)	117 / 159 (73.58%)
occurrences (all)	450	478	530
General disorders and administration site conditions			
Chills			
subjects affected / exposed	40 / 134 (29.85%)	62 / 151 (41.06%)	70 / 159 (44.03%)
occurrences (all)	136	173	208
Fatigue			
subjects affected / exposed	98 / 134 (73.13%)	105 / 151 (69.54%)	120 / 159 (75.47%)
occurrences (all)	533	559	633
Injection site erythema			
subjects affected / exposed	80 / 134 (59.70%)	89 / 151 (58.94%)	97 / 159 (61.01%)
occurrences (all)	268	284	398
Injection site induration			
subjects affected / exposed	53 / 134 (39.55%)	70 / 151 (46.36%)	85 / 159 (53.46%)
occurrences (all)	176	248	458
Injection site pain			
subjects affected / exposed	129 / 134 (96.27%)	148 / 151 (98.01%)	154 / 159 (96.86%)
occurrences (all)	1065	1087	1592
Pyrexia			
subjects affected / exposed	13 / 134 (9.70%)	25 / 151 (16.56%)	26 / 159 (16.35%)
occurrences (all)	16	33	32
Gastrointestinal disorders			

Abdominal pain upper			
subjects affected / exposed	5 / 134 (3.73%)	9 / 151 (5.96%)	9 / 159 (5.66%)
occurrences (all)	6	12	12
Nausea			
subjects affected / exposed	47 / 134 (35.07%)	56 / 151 (37.09%)	62 / 159 (38.99%)
occurrences (all)	85	167	149
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 134 (0.75%)	1 / 151 (0.66%)	3 / 159 (1.89%)
occurrences (all)	1	1	3
Oropharyngeal pain			
subjects affected / exposed	7 / 134 (5.22%)	5 / 151 (3.31%)	7 / 159 (4.40%)
occurrences (all)	9	6	8
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	54 / 134 (40.30%)	65 / 151 (43.05%)	81 / 159 (50.94%)
occurrences (all)	178	213	244
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	9 / 134 (6.72%)	10 / 151 (6.62%)	10 / 159 (6.29%)
occurrences (all)	11	12	10
Nasopharyngitis			
subjects affected / exposed	21 / 134 (15.67%)	24 / 151 (15.89%)	25 / 159 (15.72%)
occurrences (all)	38	34	44
Pharyngitis			
subjects affected / exposed	8 / 134 (5.97%)	11 / 151 (7.28%)	15 / 159 (9.43%)
occurrences (all)	8	14	15
Rhinitis			
subjects affected / exposed	6 / 134 (4.48%)	5 / 151 (3.31%)	11 / 159 (6.92%)
occurrences (all)	6	5	14
Tonsillitis			
subjects affected / exposed	6 / 134 (4.48%)	9 / 151 (5.96%)	5 / 159 (3.14%)
occurrences (all)	8	10	5
Upper respiratory tract infection			
subjects affected / exposed	31 / 134 (23.13%)	35 / 151 (23.18%)	37 / 159 (23.27%)
occurrences (all)	46	51	51

Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	43 / 134 (32.09%) 91	45 / 151 (29.80%) 131	52 / 159 (32.70%) 121

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 April 2014	The protocol was amended primarily to address comments from CBER on the previous version of the protocol, relating to addition of secondary immunogenicity objective and inclusion of detail on safety data collection and randomization procedures. Additional changes were made to ensure that the subjects/parents/legal guardians were encouraged to contact sites during the entire study in case medically-attended AEs or any AEs which was perceived as being of concern. Additionally the placebo was provided as ampoules instead of the vials and the protocol text was amended accordingly.
03 February 2015	The protocol was amended to further clarify certain sections and to correct the content errors/typographical errors which were recognized in the protocol version 3.0.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported