Clinical trial results:
A Phase 3b, Open-Label, Randomized, Multicenter Study to Assess the Safety and Immunogenicity of GlaxoSmithKline Biologicals Meningococcal group B Vaccine When Administered Concomitantly with GlaxoSmithKline Biologicals MenACWY Conjugate Vaccine to Healthy Infants

Summary

EudraCT number	2016-005117-44
Trial protocol	Outside EU/EEA
Global end of trial date	14 October 2016

Results information

Result version number	v1
This version publication date	22 October 2017
First version publication date	22 October 2017

Trial information

Trial identification

Sponsor protocol code	205240

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02106390
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	11 August 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 October 2016
Global end of trial reached?	Yes
Global end of trial date	14 October 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this trial was to assess the immunological non-inferiority of rMenB+OMV NZ and MenACWY when concomitantly administered compared to either alone in healthy infants at 3, 5, 7 and 13 months of age, as measured by the ratio of hSBA Geometric Mean Titers (GMTs) against each of the serogroup B indicator strains (for rMenB+OMV NZ) and serogroups A, C, W-135 and Y (for MenACWY) at one month after the fourth vaccination.

Protection of trial subjects:

The subjects were observed closely for at least 30 minutes following the administration of vaccine(s), with appropriate medical treatment readily available in case of a rare anaphylactic reaction.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 June 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	Argentina: 163
Country: Number of subjects enrolled	Mexico: 587
Worldwide total number of subjects	750
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	750
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

750 healthy infants, aged 3 months were recruited from 3 sites in Argentina and 4 sites in Mexico.

Pre-assignment

Screening details:

All enrolled subjects were included in the study.

Period 1

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

Blinding implementation details:

This trial is designed as an open-label trial; therefore, no blinding procedures were used.

Arms

Are arms mutually exclusive?	Yes
Arm title	rMenB+ACWY Group

Arm description:

Approximately 250 healthy infants aged 3 months who received 4 doses of rMenB + OMV NZ / MenACWY vaccines, concomitantly administered at 3, 5, 7 and 13 months of age.

Arm type	Experimental
Investigational medicinal product name	GlaxoSmithKline Biologicals Meningococcal group B Vaccine
Investigational medicinal product code	
Other name	rMenB+OMV NZ; Bexsero
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 mL pre-filled syringe. The volume delivered in a single dose was 0.5 mL.

Investigational medicinal product name	GlaxoSmithKline Biologicals Meningococcal ACWY Conjugate Vaccine
Investigational medicinal product code	
Other name	MenACWY; Menveo
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Powder (vial) + Solution (syringe or vial). The volume delivered after reconstitution was 0.5 mL.

Arm title	rMenB Group

Arm description:

Approximately 250 healthy infants aged 3 months who received 4 doses of rMenB + OMV NZ administered at 3, 5, 7 and 13 months of age.

Arm type	Active comparator
Investigational medicinal product name	GlaxoSmithKline Biologicals Meningococcal group B Vaccine
Investigational medicinal product code	
Other name	rMenB+OMV NZ; Bexsero
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 mL pre-filled syringe. The volume delivered in a single dose was 0.5 mL.

Arm title	MenACWY Group

Arm description:

Approximately 250 healthy infants aged 3 months who received 4 doses of MenACWY administered at 3, 5, 7 and 13 months of age.

Arm type	Active comparator
Investigational medicinal product name	GlaxoSmithKline Biologicals Meningococcal ACWY Conjugate Vaccine
Investigational medicinal product code	
Other name	MenACWY; Menveo
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Powder (vial) + Solution (syringe or vial). The volume delivered after reconstitution was 0.5 mL.

Number of subjects in period 1	rMenB+ACWY Group	rMenB Group	MenACWY Group
Started	252	250	248
Completed	203	202	205
Not completed	49	48	43
Consent withdrawn by subject	15	16	15
Adverse event, non-fatal	-	2	1
Unspecified	1	4	2
Lost to follow-up	25	20	13
Administrative reason	8	5	12
Protocol deviation	-	1	-

Baseline characteristics

Reporting groups	
Reporting group title	rMenB+ACWY Group
Reporting group description:	
Approximately 250 healthy infants aged 3 months who received 4 doses of rMenB + OMV NZ / MenACWY vaccines, concomitantly administered at 3, 5, 7 and 13 months of age.	
Reporting group title	rMenB Group
Reporting group description:	
Approximately 250 healthy infants aged 3 months who received 4 doses of rMenB + OMV NZ administered at 3, 5, 7 and 13 months of age.	
Reporting group title	MenACWY Group
Reporting group description:	
Approximately 250 healthy infants aged 3 months who received 4 doses of MenACWY administered at 3, 5, 7 and 13 months of age.	

Reporting group values	rMenB+ACWY Group	rMenB Group	MenACWY Group
Number of subjects	252	250	248
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)	252	250	248
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: days			
arithmetic mean	104.0	101.4	102.7
standard deviation	± 10.72	± 10.57	± 10.9
Gender categorical Units: Subjects			
Female	120	118	139
Male	132	132	109
Race/Ethnicity Units: Subjects			
White	17	20	17
Other	235	230	231

Reporting group values	Total		
Number of subjects	750		
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)	750		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Age continuous			
Units: days			
arithmetic mean			
standard deviation	-		
Gender categorical Units: Subjects			
Female	377		
Male	373		
Race/Ethnicity			
Units: Subjects			
White	54		
Other	696		

End points

End points reporting groups

Reporting group title	rMenB+ACWY Group
Reporting group description:	
Approximately 250 healthy infants aged 3 months who received 4 doses of rMenB + OMV NZ / MenACWY vaccines, concomitantly administered at 3, 5, 7 and 13 months of age.	
Reporting group title	rMenB Group
Reporting group description:	
Approximately 250 healthy infants aged 3 months who received 4 doses of rMenB + OMV NZ administered at 3, 5, 7 and 13 months of age.	
Reporting group title	MenACWY Group
Reporting group description:	
Approximately 250 healthy infants aged 3 months who received 4 doses of MenACWY administered at 3, 5, 7 and 13 months of age.	

Primary: Human Serum Bactericidal Activity (hSBA) Geometric Mean Titers (GMTs) against each of the serogroup B indicator strains

End point title	Human Serum Bactericidal Activity (hSBA) Geometric Mean Titers (GMTs) against each of the serogroup B indicator strains[1]
End point description:	
Human serum bactericidal activity (hSBA) titers against each of the serogroup B indicator strains H44/76, 5/99, NZ98/254 and M10713 after receiving 4 doses of rMenB+OMV NZ/MenACWY vaccines, concomitantly administered, versus corresponding response in subjects who received rMenB+OMV NZ administered alone, were presented in terms of vaccine group specific geometric mean titers (GMTs). This outcome measure applies only to rMenB+ACWY and rMenB groups as the serogroup B indicator strains were assessed only for these two groups. The analysis was done on the Per Protocol Set (PPS).	
End point type	Primary
End point timeframe:	
At Day 331	

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+ACWY Group	rMenB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	148	158		
Units: Titers				
geometric mean (confidence interval 95%)				
H44/76 (N=115;153)	92 (67 to 128)	104 (77 to 141)		
5/99 (N=113;148)	1850 (1122 to 3050)	1790 (1128 to 2842)		
NZ98/254 (N=148;158)	39 (29 to 53)	38 (28 to 52)		
M10713 (N=131;157)	13 (7.82 to 21)	12 (7.72 to 20)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The comparison of adjusted GMTs ratio (rMenB+OMV NZ + MenACWY versus rMenB+OMV NZ) was performed for the H44/76 serogroup B indicator strain, at one month after the fourth vaccination.

Comparison groups	rMenB+ACWY Group v rMenB Group
Number of subjects included in analysis	306
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
Method	ANOVA
Parameter estimate	GMT ratio
Point estimate	0.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	1.1

Notes:

[2] - Non-inferiority was to be concluded if, at one month following the fourth vaccination, the lower limits of the two-sided 95% confidence interval for the between-group ratios of GMTs (rMenB+OMV NZ + MenACWY versus rMenB+OMV NZ is > 0.5 for all serogroup B indicator strains.

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

The comparison of adjusted GMTs ratio (rMenB+OMV NZ + MenACWY versus rMenB+OMV NZ) was performed for the 5/99 serogroup B indicator strain, at one month after the fourth vaccination.

Comparison groups	rMenB+ACWY Group v rMenB Group
Number of subjects included in analysis	306
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
Method	ANOVA
Parameter estimate	GMT ratio
Point estimate	1.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.74
upper limit	1.45

Notes:

[3] - Non-inferiority was to be concluded if, at one month following the fourth vaccination, the lower limits of the two-sided 95% confidence interval for the between-group ratios of GMTs (rMenB+OMV NZ + MenACWY versus rMenB+OMV NZ is > 0.5 for all serogroup B indicator strains.

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

The comparison of adjusted GMTs ratio (rMenB+OMV NZ + MenACWY versus rMenB+OMV NZ) was performed for the NZ98/254 serogroup B indicator strain, at one month after the fourth vaccination.

Comparison groups	rMenB+ACWY Group v rMenB Group
Number of subjects included in analysis	306
Analysis specification	Pre-specified
Analysis type	non-inferiority[4]
Method	ANOVA
Parameter estimate	GMT ratio
Point estimate	1.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.82
upper limit	1.25

Notes:

[4] - Non-inferiority was to be concluded if, at one month following the fourth vaccination, the lower limits of the two-sided 95% confidence interval for the between-group ratios of GMTs (rMenB+OMV NZ + MenACWY versus rMenB+OMV NZ is > 0.5 for all serogroup B indicator strains.

Statistical analysis title	Statistical analysis 4

Statistical analysis description:

The comparison of adjusted GMTs ratio (rMenB+OMV NZ + MenACWY versus rMenB+OMV NZ) was performed for the M10713 serogroup B indicator strain, at one month after the fourth vaccination.

Comparison groups	rMenB+ACWY Group v rMenB Group
Number of subjects included in analysis	306
Analysis specification	Pre-specified
Analysis type	non-inferiority[5]
Method	ANOVA
Parameter estimate	GMT ratio
Point estimate	1.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.77
upper limit	1.4

Notes:

[5] - Non-inferiority was to be concluded if, at one month following the fourth vaccination, the lower limits of the two-sided 95% confidence interval for the between-group ratios of GMTs (rMenB+OMV NZ + MenACWY versus rMenB+OMV NZ is > 0.5 for all serogroup B indicator strains.

Primary: hSBA Geometric Mean Titers against each of the serogroups A, C, W-135 and Y

End point title	hSBA Geometric Mean Titers against each of the serogroups A, C, W-135 and Y[6]

End point description:

hSBA titers against N. meningitidis serogroups A, C, W-135 and Y after receiving four doses of either rMenB+OMV NZ/MenACWY concomitantly administered versus corresponding response in subjects who received MenACWY administered alone were presented in terms of vaccine group specific GMTs. This outcome measure applies only to rMenB+ACWY and MenACWY groups as the A, C, W-135 and Y serogroups were assessed only for these two groups. The analysis was done on the PPS.

End point type	Primary

End point timeframe:

At Day 331

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	rMenB+ACWY Group	MenACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	161	156		
Units: Titers				
geometric mean (confidence interval 95%)				
Serogroup A (N=159;156)	409 (300 to 556)	165 (122 to 224)		
Serogroup C (N=157;149)	452 (312 to 655)	421 (294 to 602)		
Serogroup W (N=144;143)	721 (493 to 1053)	536 (370 to 776)		
Serogroup Y (N=161;156)	410 (293 to 575)	391 (280 to 546)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

The comparison of adjusted GMTs ratio (rMenB+OMV NZ + MenACWY versus MenACWY) was performed for serogroup A, at one month after the fourth vaccination.

Comparison groups	MenACWY Group v rMenB+ACWY Group
Number of subjects included in analysis	317
Analysis specification	Pre-specified
Analysis type	non-inferiority[7]
Method	ANOVA
Parameter estimate	GMT ratio
Point estimate	2.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.97
upper limit	3.11

Notes:

[7] - Non-inferiority was to be concluded if, at one month following the fourth vaccination, the lower limits of the two-sided 95% confidence interval for the between-group ratios of GMTs (rMenB+OMV NZ + MenACWY versus MenACWY) was > 0.5 for all serogroups A, C, W-135 and Y.

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

The comparison of adjusted GMTs ratio (rMenB+OMV NZ + MenACWY versus MenACWY) was performed for serogroup C, at one month after the fourth vaccination.

Comparison groups	MenACWY Group v rMenB+ACWY Group

Number of subjects included in analysis	317
Analysis specification	Pre-specified
Analysis type	non-inferiority[8]
Method	ANOVA
Parameter estimate	GMT ratio
Point estimate	1.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.83
upper limit	1.38

Notes:

[8] - Non-inferiority was to be concluded if, at one month following the fourth vaccination, the lower limits of the two-sided 95% confidence interval for the between-group ratios of GMTs (rMenB+OMV NZ + MenACWY versus MenACWY) was > 0.5 for all serogroups A, C, W-135 and Y.

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

The comparison of adjusted GMTs ratio (rMenB+OMV NZ + MenACWY versus MenACWY) was performed for serogroup W-135, at one month after the fourth vaccination.

Comparison groups	MenACWY Group v rMenB+ACWY Group
Number of subjects included in analysis	317
Analysis specification	Pre-specified
Analysis type	non-inferiority[9]
Method	ANOVA
Parameter estimate	GMT ratio
Point estimate	1.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.04
upper limit	1.74

Notes:

[9] - Non-inferiority was to be concluded if, at one month following the fourth vaccination, the lower limits of the two-sided 95% confidence interval for the between-group ratios of GMTs (rMenB+OMV NZ + MenACWY versus MenACWY) was > 0.5 for all serogroups A, C, W-135 and Y.

Statistical analysis title	Statistical analysis 4

Statistical analysis description:

The comparison of adjusted GMTs ratio (rMenB+OMV NZ + MenACWY versus MenACWY) was performed for serogroup Y, at one month after the fourth vaccination.

Comparison groups	MenACWY Group v rMenB+ACWY Group
Number of subjects included in analysis	317
Analysis specification	Pre-specified
Analysis type	non-inferiority[10]
Method	ANOVA
Parameter estimate	GMT ratio
Point estimate	1.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.82
upper limit	1.35

Notes:

[10] - Non-inferiority was to be concluded if, at one month following the fourth vaccination, the lower limits of the two-sided 95% confidence interval for the between-group ratios of GMTs (rMenB+OMV NZ + MenACWY versus MenACWY) was > 0.5 for all serogroups A, C, W-135 and Y.

Secondary: hSBA Geometric Mean Titers against each of the serogroup B indicator strains

End point title	hSBA Geometric Mean Titers against each of the serogroup B indicator strains[11]

End point description:

hSBA GMTs against each of the N. meningitidis serogroup B indicator strains H44/76, 5/99, NZ98/254 and M10713 at baseline (Day 1). This outcome measure applies only to rMenB+ACWY and rMenB groups as the serogroup B strains were assessed only for these two groups. Analysis was performed on the Full Analysis Set (FAS).

End point type	Secondary

End point timeframe:

At Day 1

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: 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+ACWY Group	rMenB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	191	206		
Units: Titers				
geometric mean (confidence interval 95%)				
H44/76 (N=162;198)	1.03 (0.99 to 1.08)	1.02 (0.98 to 1.07)		
5/99 (N=157;192)	1.09 (0.99 to 1.21)	1.07 (0.97 to 1.17)		
NZ98/254 (N=191;206)	1.06 (1.01 to 1.12)	1.07 (1.02 to 1.12)		
M10713 (N=182;203)	1.88 (1.51 to 2.34)	1.59 (1.29 to 1.96)		

Statistical analyses

No statistical analyses for this end point

Secondary: hSBA Geometric Mean Titers against each of the serogroup B indicator strains

End point title	hSBA Geometric Mean Titers against each of the serogroup B indicator strains[12]

End point description:

hSBA GMTs against each of the N. meningitidis serogroup B indicator strains H44/76, 5/99, NZ98/254 and M10713 at one month after the third vaccination (Day 151). This outcome measure applies only to rMenB+ACWY and rMenB groups as the serogroup B strains were assessed only for these two groups. Analysis was performed on the FAS.

End point type	Secondary

End point timeframe:

At Day 151

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: 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+ACWY Group	rMenB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	181	206		
Units: Titers				
geometric mean (confidence interval 95%)				
H44/76 (N=149;199)	116 (100 to 135)	129 (113 to 147)		
5/99 (N=137;188)	891 (752 to 1055)	935 (803 to 1088)		
NZ98/254 (N=181;205)	32 (26 to 39)	33 (27 to 40)		
M10713 (N=168;206)	9.09 (6.57 to 13)	10 (7.50 to 14)		

Statistical analyses

No statistical analyses for this end point

Secondary: hSBA Geometric Mean Titers against each of the serogroup B indicator strains

End point title	hSBA Geometric Mean Titers against each of the serogroup B indicator strains[13]

End point description:

hSBA GMTs against each of the N. meningitidis serogroup B indicator strains H44/76, 5/99, NZ98/254 and M10713 before the fourth vaccination (Day 301). This outcome measure applies only to rMenB+ACWY and rMenB groups as the serogroup B strains were assessed only for these two groups. Analysis was performed on the FAS.

End point type	Secondary

End point timeframe:

At Day 301

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: 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+ACWY Group	rMenB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	173	204		
Units: Titers				
geometric mean (confidence interval 95%)				
H44/76 (N=130;190)	7.68 (5.91 to 9.99)	8.31 (6.54 to 11)		
5/99 (N=139;189)	131 (107 to 161)	109 (90 to 132)		
NZ98/254 (N=173;204)	3.21 (2.44 to 4.21)	2.93 (2.25 to 3.81)		
M10713 (N=151;198)	2.48 (1.89 to 3.27)	2.40 (1.85 to 3.10)		

Statistical analyses

No statistical analyses for this end point

Secondary: hSBA Geometric Mean Titers against each of the serogroup B indicator strains

End point title	hSBA Geometric Mean Titers against each of the serogroup B indicator strains[14]

End point description:

hSBA GMTs against each of the N. meningitidis serogroup B indicator strains H44/76, 5/99, NZ98/254 and M10713 at one month after the fourth vaccination (Day 331). This outcome measure applies only to rMenB+ACWY and rMenB groups as the serogroup B strains were assessed only for these two groups. Analysis was performed on the FAS.

End point type	Secondary

End point timeframe:

At Day 331

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: 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+ACWY Group	rMenB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	181	196		
Units: Titers				
geometric mean (confidence interval 95%)				
H44/76 (N=141;188)	122 (98 to 151)	126 (104 to 154)		
5/99 (N=143;183)	1404 (1016 to 1939)	1262 (934 to 1706)		
NZ98/254 (N=181;196)	37 (30 to 45)	36 (30 to 44)		
M10713 (N=161;194)	18 (14 to 24)	17 (13 to 22)		

Statistical analyses

No statistical analyses for this end point

Secondary: hSBA Geometric Mean Titers against each of the serogroups A, C, W-135 and Y

End point title	hSBA Geometric Mean Titers against each of the serogroups A, C, W-135 and Y[15]

End point description:

hSBA GMTs against each of the N. meningitidis serogroups A, C, W-135 and Y at baseline (Day 1). This outcome measure applies only to rMenB+ACWY and MenACWY groups as the serogroups A, C, W-135 and Y were assessed only for these two groups. Analysis was performed on the FAS.

End point type	Secondary

End point timeframe:

At Day 1

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: 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+ACWY Group	MenACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	213	210		
Units: Titers				
geometric mean (confidence interval 95%)				
Serogroup A (N=211;206)	2.05 (1.97 to 2.15)	2.08 (1.99 to 2.17)		
Serogroup C (N=206;204)	2.16 (1.98 to 2.35)	2.09 (1.92 to 2.27)		
Serogroup W (N=194;196)	2.33 (2.13 to 2.55)	2.31 (2.11 to 2.52)		
Serogroup Y (N=213;210)	2.06 (1.95 to 2.17)	2.16 (2.05 to 2.28)		

Statistical analyses

No statistical analyses for this end point

Secondary: hSBA Geometric Mean Titers against each of the serogroups A, C, W-135 and Y

End point title	hSBA Geometric Mean Titers against each of the serogroups A, C, W-135 and Y[16]

End point description:

hSBA GMTs against each of the N. meningitidis serogroups A, C, W-135 and Y at one month after the third vaccination (Day 151). This outcome measure applies only to rMenB+ACWY and MenACWY groups as the serogroups A, C, W-135 and Y were assessed only for these two groups. Analysis was performed on the FAS.

End point type	Secondary

End point timeframe:

At Day 151

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: 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+ACWY Group	MenACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	215	214		
Units: Titers				
geometric mean (confidence interval 95%)				
Serogroup A (N=214;210)	303 (242 to 379)	136 (108 to 169)		
Serogroup C (N=208;204)	388 (320 to 469)	416 (345 to 502)		
Serogroup W (N=178;188)	347 (282 to 427)	298 (244 to 364)		
Serogroup Y (N=215;214)	226 (182 to 282)	283 (228 to 351)		

Statistical analyses

No statistical analyses for this end point

Secondary: hSBA Geometric Mean Titers against each of the serogroups A, C, W-135 and Y

End point title	hSBA Geometric Mean Titers against each of the serogroups A, C, W-135 and Y[17]

End point description:

hSBA GMTs against each of the N. meningitidis serogroups A, C, W-135 and Y before the fourth vaccination (Day 301). This outcome measure applies only to rMenB+ACWY and MenACWY groups as the serogroups A, C, W-135 and Y were assessed only for these two groups. Analysis was performed on the FAS.

End point type	Secondary

End point timeframe:

At Day 301

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: 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+ACWY Group	MenACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	203	204		
Units: Titers				
geometric mean (confidence interval 95%)				
Serogroup A (N=200;200)	20 (15 to 28)	15 (11 to 21)		
Serogroup C (N=196;189)	31 (23 to 41)	43 (32 to 58)		
Serogroup W (N=169;178)	48 (37 to 63)	47 (36 to 62)		
Serogroup Y (N=203;204)	38 (30 to 49)	43 (33 to 55)		

Statistical analyses

No statistical analyses for this end point

Secondary: hSBA Geometric Mean Titers against each of the serogroups A, C, W-135 and Y

End point title	hSBA Geometric Mean Titers against each of the serogroups A, C, W-135 and Y[18]

End point description:

hSBA GMTs against each of the N.meningitidis serogroups A, C, W-135 and Y at one month after the fourth vaccination (Day 331). This outcome measure applies only to rMenB+ACWY and MenACWY groups as the serogroups A, C, W-135 and Y were assessed only for these two groups. Analysis was performed on the FAS.

End point type	Secondary

End point timeframe:

At Day 331

Notes:

[18] - 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+ACWY Group	MenACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	199	204		
Units: Titers				
geometric mean (confidence interval 95%)				
Serogroup A (N=197;203)	329 (269 to 403)	132 (108 to 161)		
Serogroup C (N=193;194)	331 (268 to 409)	311 (252 to 384)		
Serogroup W (N=179;184)	576 (458 to 723)	428 (342 to 537)		
Serogroup Y (N=199;204)	377 (304 to 466)	363 (294 to 448)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with hSBA titers ≥1:5 against each of the serogroup B indicator strains

End point title	Percentage of subjects with hSBA titers ≥1:5 against each of the serogroup B indicator strains[19]

End point description:

Percentage of subjects with hSBA titers ≥ 1:5 against each of the N. meningitidis serogroup B indicator strains H44/76, 5/99, NZ98/254 and M10713 before the first vaccination (Day 1). This outcome measure applies only rMenB+ACWY and rMenB groups as the serogroup B strains were assessed only for these two groups. Analysis was performed on the FAS.

End point type	Secondary

End point timeframe:

At Day 1

Notes:

[19] - 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+ACWY Group	rMenB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	191	206		
Units: Percentage of subjects				
number (confidence interval 95%)				
H44/76 (N=162;198)	0 (0.0 to 2.3)	1 (0.01 to 2.8)		
5/99 (N=157;192)	1 (0.15 to 4.5)	1 (0.13 to 3.7)		
NZ98/254 (N=191;206)	1 (0.01 to 2.9)	1 (0.01 to 2.7)		
M10713 (N=182;203)	16 (11.4 to 22.7)	11 (6.9 to 15.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with hSBA titers ≥1:5 against each of the serogroup B indicator strains

End point title	Percentage of subjects with hSBA titers ≥1:5 against each of the serogroup B indicator strains[20]

End point description:

Percentage of subjects with hSBA titers ≥ 1:5 against each of the N. meningitidis serogroup B indicator strains H44/76, 5/99, NZ98/254 and M10713 one month after the third vaccination (Day 151). This outcome measure applies only to rMenB+ACWY and rMenB groups as the serogroup B indicator strains were assessed only for these two groups. Analysis was performed on the FAS.

End point type	Secondary

End point timeframe:

At Day 151

Notes:

[20] - 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+ACWY Group	rMenB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	181	206		
Units: Percentage of subjects				
number (confidence interval 95%)				
H44/76 (N=149;199)	100 (97.6 to 100.0)	100 (98.2 to 100.0)		
5/99 (N=137;188)	100 (97.3 to 100.0)	100 (98.1 to 100.0)		
NZ98/254 (N=181;205)	96 (92.2 to 98.4)	97 (93.7 to 98.9)		
M10713 (N=168;206)	70 (62.7 to 77.0)	68 (61.1 to 74.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with hSBA titers ≥1:5 against each of the serogroup B strains

End point title	Percentage of subjects with hSBA titers ≥1:5 against each of the serogroup B strains[21]

End point description:

Percentage of subjects with hSBA titers ≥ 1:5 against each of the N. meningitidis serogroup B indicator strains H44/76, 5/99, NZ98/254 and M10713 before the fourth vaccination (Day 301). This outcome measure applies only to rMenB+ACWY and rMenB groups as the serogroup B indicator strains were assessed only for these two groups. Analysis was performed on the FAS.

End point type	Secondary

End point timeframe:

At Day 301

Notes:

[21] - 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+ACWY Group	rMenB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	173	204		
Units: Percentage of subjects				
number (confidence interval 95%)				
H44/76 (N=130;190)	74 (65.4 to 81.2)	75 (67.9 to 80.7)		

5/99 (N=139;189)	100 (97.4 to 100.0)	97 (93.9 to 99.1)		
NZ98/254 (N=173;204)	42 (34.2 to 49.3)	36 (29.7 to 43.3)		
M10713 (N=151;198)	33 (25.7 to 41.2)	31 (24.5 to 37.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with hSBA titers ≥1:5 against each of the serogroup B strains

End point title	Percentage of subjects with hSBA titers ≥1:5 against each of the serogroup B strains[22]

End point description:

Percentage of subjects with hSBA titers ≥ 1:5 against each of the N. meningitidis serogroup B indicator strains H44/76, 5/99, NZ98/254 and M10713 one month after the fourth vaccination (Day 331). This outcome measure applies only to rMenB+ACWY and rMenB groups as the serogroup B indicator strains were assessed only for these two groups. Analysis was performed on the FAS.

End point type	Secondary

End point timeframe:

At Day 331

Notes:

[22] - 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+ACWY Group	rMenB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	181	196		
Units: Percentage of subjects				
number (confidence interval 95%)				
H44/76 (N=141;188)	100 (97.4 to 100.0)	99 (97.1 to 99.99)		
5/99 (N=143;183)	99 (95.0 to 99.83)	97 (93.0 to 98.8)		
NZ98/254 (N=181;196)	100 (98.0 to 100.0)	98 (94.9 to 99.4)		
M10713 (N=161;194)	87 (80.8 to 91.7)	87 (81.6 to 91.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with hSBA titers ≥1:8 against each of the serogroup B indicator strains

End point title	Percentage of subjects with hSBA titers ≥1:8 against each of the serogroup B indicator strains[23]

End point description:

Percentage of subjects with hSBA titers ≥ 1:8 against each of the N. meningitidis serogroup B indicator strains H44/76, 5/99, NZ98/254 and M10713 at baseline (Day 1). This outcome measure applies only to rMenB+ACWY and rMenB groups as the serogroup B indicator strains were assessed only for these two groups. Analysis was performed on the FAS.

End point type	Secondary

End point timeframe:

At Day 1

Notes:

[23] - 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+ACWY Group	rMenB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	191	206		
Units: Percentage of subjects				
number (confidence interval 95%)				
H44/76 (N=162;198)	0 (0.0 to 2.3)	0 (0.0 to 1.8)		
5/99 (N=157;192)	1 (0.02 to 3.5)	1 (0.01 to 2.9)		
NZ98/254 (N=191;206)	1 (0.01 to 2.9)	1 (0.01 to 2.7)		
M10713 (N=182;203)	12 (7.3 to 17.1)	8 (4.6 to 12.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with hSBA titers ≥1:8 against each of the serogroup B indicator strains

End point title	Percentage of subjects with hSBA titers ≥1:8 against each of the serogroup B indicator strains[24]

End point description:

Percentage of subjects with hSBA titers ≥ 1:8 against each of the N. meningitidis serogroup B indicator strains H44/76, 5/99, NZ98/254 and M10713 at one month after third vaccination (Day 151). This outcome measure applies only to rMenB+ACWY and rMenB groups as the serogroup B indicator strains were assessed only for these two groups. Analysis was performed on the FAS.

End point type	Secondary

End point timeframe:

At Day 151

Notes:

[24] - 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+ACWY Group	rMenB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	181	206		
Units: Percentage of subjects				
number (confidence interval 95%)				
H44/76 (N=149;199)	100 (97.6 to 100.0)	100 (98.2 to 100.0)		
5/99 (N=137;188)	100 (97.3 to 100.0)	100 (98.1 to 100.0)		
NZ98/254 (N=181;205)	92 (87.4 to 95.7)	92 (87.6 to 95.5)		
M10713 (N=168;206)	65 (57.2 to 72.1)	59 (52.2 to 66.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with hSBA titers ≥1:8 against each of the serogroup B indicator strains

End point title	Percentage of subjects with hSBA titers ≥1:8 against each of the serogroup B indicator strains[25]

End point description:

Percentage of subjects with hSBA titers ≥ 1:8 against each of the N. meningitidis serogroup B indicator strains H44/76, 5/99, NZ98/254 and M10713 before the fourth vaccination (Day 301). This outcome measure applies only to rMenB+ACWY and rMenB groups as the serogroup B indicator strains were assessed only for these two groups. Analysis was performed on the FAS.

End point type	Secondary

End point timeframe:

At Day 301

Notes:

[25] - 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+ACWY Group	rMenB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	173	204		
Units: Percentage of subjects				
number (confidence interval 95%)				
H44/76 (N=130;190)	58 (49.5 to 67.0)	56 (48.9 to 63.5)		
5/99 (N=139;189)	100 (97.4 to 100.0)	97 (93.2 to 98.8)		
NZ98/254 (N=173;204)	26 (19.6 to 33.2)	26 (20.6 to 33.1)		
M10713 (N=151;198)	21 (14.4 to 27.9)	23 (17.5 to 29.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with hSBA titers ≥1:8 against each of the serogroup B indicator strains

End point title	Percentage of subjects with hSBA titers ≥1:8 against each of the serogroup B indicator strains[26]

End point description:

Percentage of subjects with hSBA titers ≥ 1:8 against each of the N. meningitidis serogroup B indicator strains H44/76, 5/99, NZ98/254 and M10713 at one month after the fourth vaccination (Day 331). This outcome measure applies only rMenB+ACWY and rMenB groups as the serogroup B indicator strains were assessed only for these two groups. Analysis was performed on the FAS.

End point type	Secondary

End point timeframe:

At Day 331

Notes:

[26] - 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+ACWY Group	rMenB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	181	196		
Units: Percentage of subjects				
number (confidence interval 95%)				
H44/76 (N=141;188)	100 (97.4 to 100.0)	99 (97.1 to 99.99)		
5/99 (N=143;183)	99 (95.0 to 99.83)	97 (93.0 to 98.8)		
NZ98/254 (N=181;196)	98 (94.4 to 99.4)	94 (90.2 to 97.2)		
M10713 (N=161;194)	83 (76.5 to 88.6)	82 (76.4 to 87.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with hSBA titers ≥1:4 against each of the serogroups A, C, W-135 and Y

End point title	Percentage of subjects with hSBA titers ≥1:4 against each of the serogroups A, C, W-135 and Y[27]

End point description:

Percentage of subjects with hSBA titers ≥ 1:4 against each of the N. meningitidis serogroups A, C, W-135 and Y before the first vaccination (Day 1). This outcome measure applies only to rMenB+ACWY and MenACWY groups as the A, C, W-135 and Y serogroups were assessed only for these two groups. Analysis was performed on the FAS.

End point type	Secondary

End point timeframe:

At Day 1

Notes:

[27] - 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+ACWY Group	MenACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	213	210		
Units: Percentage of subjects				
number (confidence interval 95%)				
Serogroup A (N=211;206)	1 (0.11 to 3.4)	1 (0.12 to 3.5)		
Serogroup C (N=206;204)	4 (1.7 to 7.5)	3 (1.4 to 6.9)		
Serogroup W (N=194;196)	4 (1.8 to 8.0)	4 (1.4 to 7.2)		
Serogroup Y (N=213;210)	2 (0.5 to 4.7)	5 (2.3 to 8.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with hSBA titers ≥1:4 against each of the serogroups A, C, W-135 and Y

End point title	Percentage of subjects with hSBA titers ≥1:4 against each of the serogroups A, C, W-135 and Y[28]

End point description:

Percentage of subjects with hSBA titers ≥ 1:4 against each of the N. meningitidis serogroups A, C, W-135 and Y at one month after the third vaccination (Day 151). This outcome measure applies only to rMenB+ACWY and MenACWY groups as the A, C, W-135 and Y serogroups were assessed only for these two groups. Analysis was performed on the FAS.

End point type	Secondary

End point timeframe:

At Day 151

Notes:

[28] - 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+ACWY Group	MenACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	215	214		
Units: Percentage of subjects				
number (confidence interval 95%)				
Serogroup A (N=214;210)	99 (97.4 to 99.99)	96 (92.0 to 98.0)		
Serogroup C (N=208;204)	100 (98.2 to 100.0)	100 (98.2 to 100.0)		
Serogroup W (N=178;188)	100 (97.9 to 100.0)	100 (98.1 to 100.0)		
Serogroup Y (N=215;214)	99 (96.0 to 99.71)	100 (98.3 to 100.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with hSBA titers ≥1:4 against each of the serogroups A, C, W-135 and Y

End point title	Percentage of subjects with hSBA titers ≥1:4 against each of the serogroups A, C, W-135 and Y[29]

End point description:

Percentage of subjects with hSBA titers ≥ 1:4 against each of the N. meningitidis serogroups A, C, W-135 and Y before the fourth vaccination (Day 301). This outcome measure applies only to rMenB+ACWY and MenACWY groups as the A, C, W-135 and Y serogroups were assessed only for these two groups. Analysis was performed on the FAS.

End point type	Secondary

End point timeframe:

At Day 301

Notes:

[29] - 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+ACWY Group	MenACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	203	204		
Units: Percentage of subjects				
number (confidence interval 95%)				
Serogroup A (N=200;200)	68 (60.5 to 73.9)	63 (55.4 to 69.2)		
Serogroup C (N=196;189)	88 (82.3 to 92.0)	89 (84.1 to 93.4)		
Serogroup W (N=169;178)	93 (88.7 to 96.7)	96 (91.3 to 98.0)		
Serogroup Y (N=203;204)	91 (85.8 to 94.3)	95 (90.6 to 97.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with hSBA titers ≥1:4 against each of the serogroups A, C, W-135 and Y

End point title	Percentage of subjects with hSBA titers ≥1:4 against each of the serogroups A, C, W-135 and Y[30]

End point description:

Percentage of subjects with hSBA titers ≥ 1:4 against each of the N. meningitidis serogroups A, C, W-135 and Y at one month after the fourth vaccination (Day 331). This outcome measure applies only to rMenB+ACWY and MenACWY groups as the A, C, W-135 and Y serogroups were assessed only for these two groups. Analysis was performed on the FAS.

End point type	Secondary

End point timeframe:

At Day 331

Notes:

[30] - 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+ACWY Group	MenACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	199	204		
Units: Percentage of subjects				
number (confidence interval 95%)				
Serogroup A (N=197;203)	100 (98.1 to 100.0)	98 (94.3 to 99.2)		
Serogroup C (N=193;194)	100 (98.1 to 100.0)	100 (98.1 to 100.0)		
Serogroup W (N=179;184)	100 (98.0 to 100.0)	100 (98.0 to 100.0)		
Serogroup Y (N=199;204)	100 (98.2 to 100.0)	99 (97.3 to 99.99)		

Statistical analyses

No statistical analyses for this end point

Secondary: Within-subject Geometric Mean Ratios (GMRs) against each of the serogroup B indicator strains

End point title	Within-subject Geometric Mean Ratios (GMRs) against each of the serogroup B indicator strains[31]

End point description:

GMRs of GMTs against each of the serogroup B indicator strains H44/76, 5/99, NZ98/254 and M10713 were calculated at one month after the fourth vaccination (Day 331) versus prior to the fourth vaccination (Day 301). Analysis was performed on the FAS.

End point type	Secondary

End point timeframe:

At Day 331/Day 301

Notes:

[31] - 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+ACWY Group	rMenB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	155	195		
Units: Ratio				
geometric mean (confidence interval 95%)				
H44/76 (N=109;178)	17 (13 to 22)	16 (12 to 20)		
5/99 (N=118;169)	9.60 (6.99 to 13)	12 (8.86 to 16)		
NZ98/254 (N=155;195)	11 (8.35 to 15)	12 (9.39 to 16)		
M10713 (N=130;187)	5.99 (4.20 to 8.54)	6.75 (4.90 to 9.29)		

Statistical analyses

No statistical analyses for this end point

Secondary: Within-subject GMRs against each of serogroups A, C, W-135 and Y

End point title	Within-subject GMRs against each of serogroups A, C, W-135 and Y[32]

End point description:

GMRs of GMTs against each of serogroups A, C, W-135 and Y were calculated at one month after the fourth vaccination (Day 331) versus prior to the fourth vaccination (Day 301). Analysis was performed on the FAS.

End point type	Secondary

End point timeframe:

At Day 331/Day 301

Notes:

[32] - 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+ACWY Group	MenACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	197	201		
Units: Ratio				
geometric mean (confidence interval 95%)				
Serogroup A (N=192;196)	16 (13 to 21)	8.75 (6.69 to 11)		
Serogroup C (N=185;178)	11 (8.86 to 14)	7.79 (6.25 to 9.71)		
Serogroup W (N=155;161)	13 (10 to 16)	9.44 (7.52 to 12)		
Serogroup Y (N=197;201)	9.75 (8.00 to 12)	8.97 (7.36 to 11)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with four-fold increases in hSBA titers against each of the serogroup B indicator strains

End point title	Percentage of subjects with four-fold increases in hSBA titers against each of the serogroup B indicator strains[33]

End point description:

Percentage of subjects with four-fold increases in hSBA titers against each of the N. meningitidis serogroup B indicator strains H44/76, 5/99, NZ98/254 and M10713 at one month after the fourth vaccination (Day 331) over prior to the fourth vaccination (Day 301). This outcome measure applies only to rMenB+ACWY and rMenB groups as the serogroup B indicator strains were assessed only for these two groups. Analysis was performed on the FAS.

End point type	Secondary

End point timeframe:

At Day 331

Notes:

[33] - 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+ACWY Group	rMenB Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	167	192		
Units: Percentage of subjects				
number (confidence interval 95%)				
H44/76 (N=123;176)	100 (97.0 to 100.0)	99 (96.9 to 99.99)		
5/99 (N=118;167)	99 (95.4 to 99.98)	96 (92.3 to 98.7)		
NZ98/254 (N=167;192)	98 (94.0 to 99.3)	94 (90.0 to 97.1)		
M10713 (N=146;187)	74 (66.1 to 80.9)	76 (69.2 to 81.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with four-fold increases in hSBA titers against each of the serogroups A, C, W-135 and Y

End point title	Percentage of subjects with four-fold increases in hSBA titers against each of the serogroups A, C, W-135 and Y[34]

End point description:

Percentages of subjects with four-fold increases in hSBA titers against each of the N. meningitidis serogroups A,C,W-135 and Y at one month after the fourth vaccination (Day 331) over prior to the fourth vaccination (Day 301). This outcome measure applies only to rMenB+ACWY and MenACWY groups as the A, C, W-135 and Y serogroups were assessed only for these two groups. Analysis was performed on the FAS.

End point type	Secondary

End point timeframe:

At Day 331

Notes:

[34] - 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+ACWY Group	MenACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	197	197		
Units: Percentage of subjects				
number (confidence interval 95%)				
Serogroup A (N=194;194)	99 (97.2 to 99.99)	92 (87.6 to 95.6)		
Serogroup C (N=186;183)	98 (95.4 to 99.67)	100 (98.0 to 100.0)		
Serogroup W (N=166;168)	100 (97.8 to 100.0)	99 (95.8 to 99.86)		
Serogroup Y (N=197;197)	98 (95.6 to 99.68)	100 (98.1 to 100.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with hSBA titers ≥1:8 against each of the serogroups A, C, W-135 and Y

End point title	Percentage of subjects with hSBA titers ≥1:8 against each of the serogroups A, C, W-135 and Y[35]

End point description:

Percentage of subjects with hSBA titers ≥ 1:8 against each of the N. meningitidis serogroups A, C, W-135 and Y at baseline (Day 1). This outcome measure applies only to rMenB+ACWY and MenACWY groups as the A, C, W-135 and Y serogroups were assessed only for these two groups. Analysis was performed on the FAS.

End point type	Secondary

End point timeframe:

At Day 1

Notes:

[35] - 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+ACWY Group	MenACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	213	210		
Units: Percentage of subjects				
number (confidence interval 95%)				
Serogroup A (N=211;206)	1 (0.01 to 2.6)	1 (0.01 to 2.7)		
Serogroup C (N=206;204)	2 (0.8 to 5.6)	2 (0.5 to 4.9)		
Serogroup W (N=194;196)	4 (1.5 to 7.3)	3 (0.8 to 5.9)		
Serogroup Y (N=213;210)	0 (0.0 to 1.7)	2 (0.5 to 4.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with hSBA titers ≥1:8 against each of the serogroups A, C, W-135 and Y

End point title	Percentage of subjects with hSBA titers ≥1:8 against each of the serogroups A, C, W-135 and Y[36]

End point description:

Percentage of subjects with hSBA titers ≥ 1:8 against each of the N. meningitidis serogroups A, C, W-135 and Y at one month after the third vaccination (Day 151). This outcome measure applies only to rMenB+ACWY and MenACWY groups as the A, C, W-135 and Y serogroups were assessed only for these two groups. Analysis was performed on the FAS.

End point type	Secondary

End point timeframe:

At Day 151

Notes:

[36] - 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+ACWY Group	MenACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	215	214		
Units: Percentage of subjects				
number (confidence interval 95%)				
Serogroup A (N=214;210)	99 (97.4 to 99.99)	96 (92.0 to 98.0)		
Serogroup C (N=208;204)	100 (98.2 to 100.0)	100 (98.2 to 100.0)		
Serogroup W (N=178;188)	100 (97.9 to 100.0)	99 (97.1 to 99.99)		
Serogroup Y (N=215;214)	98 (95.3 to 99.5)	99 (97.4 to 99.99)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with hSBA titers ≥1:8 against each of the serogroups A, C, W-135 and Y

End point title	Percentage of subjects with hSBA titers ≥1:8 against each of the serogroups A, C, W-135 and Y[37]

End point description:

Percentage of subjects with hSBA titers ≥ 1:8 against each of the N. meningitidis serogroups A, C, W-135 and Y before the fourth vaccination (Day 301). This outcome measure applies only to rMenB+ACWY and MenACWY groups as the A, C, W-135 and Y serogroups were assessed only for these two groups. Analysis was performed on the FAS.

End point type	Secondary

End point timeframe:

At Day 301

Notes:

[37] - 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+ACWY Group	MenACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	203	204		
Units: Percentage of subjects				
number (confidence interval 95%)				
Serogroup A (N=200;200)	65 (58.0 to 71.6)	58 (50.8 to 64.9)		
Serogroup C (N=196;189)	77 (70.5 to 82.7)	85 (79.3 to 89.9)		
Serogroup W (N=169;178)	92 (86.5 to 95.4)	91 (85.8 to 94.8)		
Serogroup Y (N=203;204)	86 (80.1 to 90.2)	91 (85.8 to 94.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with hSBA titers ≥1:8 against each of the serogroups A, C, W-135 and Y

End point title	Percentage of subjects with hSBA titers ≥1:8 against each of the serogroups A, C, W-135 and Y[38]

End point description:

Percentage of subjects with hSBA titers ≥ 1:8 against each of the N. meningitidis serogroups A, C, W-135 and Y at one month after the fourth vaccination (Day 331). This outcome measure applies only to rMenB+ACWY and MenACWY groups as the A, C, W-135 and Y serogroups were assessed only for these two groups. Analysis was performed on the FAS.

End point type	Secondary

End point timeframe:

At Day 331

Notes:

[38] - 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+ACWY Group	MenACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	199	204		
Units: Percentage of subjects				
number (confidence interval 95%)				
Serogroup A (N=197;203)	100 (98.1 to 100.0)	96 (92.4 to 98.3)		
Serogroup C (N=193;194)	99 (97.1 to 99.99)	100 (98.1 to 100.0)		
Serogroup W (N=179;184)	100 (98.0 to 100.0)	100 (98.0 to 100.0)		
Serogroup Y (N=199;204)	98 (95.7 to 99.69)	99 (97.3 to 99.99)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with solicited local and systemic Adverse Events (AEs)

End point title	Number of subjects with solicited local and systemic Adverse Events (AEs)

End point description:

Number of subjects with solicited local and systemic AEs during the 7-days period (including the day of vaccination) after each vaccination. Analysis was performed on the solicited Safety Set.

End point type	Secondary

End point timeframe:

From Day 1 (6 hours) to Day 7 after each vaccination (Days 1, 61, 121 and 301)

End point values	rMenB+ACWY Group	rMenB Group	MenACWY Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	240	232	237	
Units: Subjects				
Any (N=240;232;237)	235	226	194	
Any local (N=240;232;237)	220	214	157	
Any Systemic (N=240;232;237)	217	217	178	
Erythema (vaccination 1) (N=239;227;232)	101	102	44	
Induration (vaccination 1) (N=239;230;233)	111	102	22	
Swelling (vaccination 1) (N=239;229;233)	82	86	22	
Tenderness (vaccination 1) (N=239;227;234)	162	159	73	
Change in Eating Habits (vacc. 1) (N=238;227;232)	53	47	34	
Diarrhea (vaccination 1) (N=237;228;234)	46	41	42	
Irritability (vaccination 1) (N=237;226;233)	111	121	87	
Persistent Crying (vaccination 1) (N=237;228;234)	124	132	85	
Rash (vaccination 1) (N=237;225;233)	19	28	18	
Sleepiness (vaccination 1) (N=238;225;232)	69	78	54	
Vomiting (vaccination 1) (N=237;228;234)	14	28	23	
Fever (vaccination 1) (N=239;229;233)	49	54	10	
Prevention of Pain/Fever (vacc.1) (N=237;228;227)	44	37	32	
Treatment of Pain/Fever (vacc.1) (N=237;228;227)	82	98	25	
Erythema (vaccination 2) (N=227;220;229)	97	102	47	
Induration (vaccination 2) (N=227;221;229)	99	110	32	
Swelling (vaccination 2) (N=227;220;229)	78	83	24	
Tenderness (vaccination 2) (N=227;221;229)	142	138	66	
Change in Eating Habits (vacc. 2) (N=226;220;229)	46	44	31	
Diarrhea (vaccination 2) (N=226;220;228)	37	36	24	
Irritability (vaccination 2) (N=226;220;228)	99	95	70	

Persistent Crying (vaccination 2) (N=226;220;228)	104	108	66	
Rash (vaccination 2) (N=226;219;228)	16	21	13	
Sleepiness (vaccination 2) (N=225;220;227)	51	55	45	
Vomiting (vaccination 2) (N=226;220;229)	10	21	17	
Fever (vaccination 2) (N=227;218;227)	48	54	15	
Prevention of Pain/Fever (vacc.2) (N=226;218;228)	33	35	17	
Treatment of Pain/Fever (vacc.2) (N=226;219;228)	74	91	29	
Erythema (vaccination 3) (N=218;215;220)	86	96	35	
Induration (vaccination 3) (N=217;215;221)	92	103	30	
Swelling (vaccination 3) (N=218;214;220)	73	82	19	
Tenderness (vaccination 3) (N=203;200;204)	139	128	59	
Change in Eating Habits (vacc. 3) (N=218;215;221)	42	45	33	
Diarrhea (vaccination 3) (N=218;215;221)	24	40	25	
Irritability (vaccination 3) (N=218;215;220)	83	84	61	
Persistent Crying (vaccination 3) (N=218;214;221)	90	92	60	
Rash (vaccination 3) (N=218;215;220)	10	11	11	
Sleepiness (vaccination 3) (N=218;215;221)	39	46	39	
Vomiting (vaccination 3) (N=218;215;221)	7	27	14	
Fever (vaccination 3) (N=218;214;222)	37	38	25	
Prevention of Pain/Fever (vacc.3) (N=217;214;222)	29	25	19	
Treatment of Pain/Fever (vacc.3) (N=217;215;222)	57	69	31	
Erythema (vaccination 4) (N=203;199;204)	73	88	37	
Induration (vaccination 4) (N=203;200;204)	84	93	29	
Swelling (vaccination 4) (N=203;200;204)	75	74	21	
Tenderness (vaccination 4) (N=203;200;204)	126	129	64	
Change in Eating Habits (vacc. 4) (N=203;200;204)	59	45	40	
Diarrhea (vaccination 4) (N=203;200;204)	29	28	23	
Irritability (vaccination 4) (N=203;200;204)	81	74	57	
Persistent Crying (vaccination 4) (N=203;200;204)	84	89	56	
Rash (vaccination 4) (N=203;200;204)	11	13	6	
Sleepiness (vaccination 4) (N=203;200;204)	50	37	33	
Vomiting (vaccination 4) (N=203;200;204)	15	14	11	
Fever (vaccination 4) (N=203;200;202)	53	46	19	

Prevention of Pain/Fever (vacc.4) (N=202;200;204)	26	26	10	
Treatment of Pain/Fever (vacc.4) (N=202;200;204)	71	67	31	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with unsolicited adverse events

End point title	Number of subjects with unsolicited adverse events

End point description:

An unsolicited adverse event (AE) is defined as any untoward medical occurrence in a subject or clinical investigation subject who was administered a pharmaceutical product at any dose that does not necessarily have to have a causal relationship with this treatment. Analysis was performed on the unsolicited Safety Set.

End point type	Secondary

End point timeframe:

From Day 1 to Day 7 after each vaccination (Days 1, 61, 121 and 301)

End point values	rMenB+ACWY Group	rMenB Group	MenACWY Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	249	249	246	
Units: Subjects				
Any AEs (N=249;249;246)	103	116	70	
Any unsolicited AEs (vaccination 1)(N=240;233;235)	63	62	20	
Any unsolicited AEs (vaccination 2)(N=230;222;229)	60	69	29	
Any unsolicited AEs (vaccination 3)(N=220;216;223)	57	63	23	
Any unsolicited AEs (vaccination 4)(N=203;202;205)	44	58	13	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with SAEs, AEs leading to withdrawal and medically attended AEs (MAEs)

End point title	Number of subjects with SAEs, AEs leading to withdrawal and medically attended AEs (MAEs)

End point description:

A serious adverse event is any untoward medical occurrence that at any dose results in death, is life threatening, requires prolonged hospitalization or results in persistent or significant disability, incapacity, congenital anomaly or birth defect. MAEs include events for which the subject received medical attention defined as hospitalization, an emergency room visit, or a visit to or from medical personnel (medical doctor) for any reason. Analysis was performed on the unsolicited Safety Set.

End point type	Secondary

End point timeframe:

Throughout the whole study period (from Day 1 up to Day 331)

End point values	rMenB+ACWY Group	rMenB Group	MenACWY Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	249	249	246	
Units: Subjects				
Any SAEs	6	13	11	
Any Medically Attended AEs	177	188	183	
Any AEs leading to premature withdrawal	0	2	1	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Solicited local and systemic symptoms: from Day 1 (6 hours) up to Day 7 after each vaccination; Unsolicited AEs: from Day 1 up to Day 7; SAEs: throughout the whole study period (from Day 1 to Day 331).	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups	
Reporting group title	rMenB+ACWY Group
Reporting group description: Approximately 250 healthy infants aged 3 months who received 4 doses of rMenB + OMV NZ / MenACWY vaccines, concomitantly administered at 3, 5, 7 and 13 months of age.	
Reporting group title	MenACWY Group
Reporting group description: Approximately 250 healthy infants aged 3 months who received 4 doses of MenACWY administered at 3, 5, 7 and 13 months of age.	
Reporting group title	rMenB Group
Reporting group description: Approximately 250 healthy infants aged 3 months who received 4 doses of rMenB + OMV NZ administered at 3, 5, 7 and 13 months of age	

Serious adverse events	rMenB+ACWY Group	MenACWY Group	rMenB Group
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 249 (2.41%)	11 / 246 (4.47%)	13 / 249 (5.22%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Limb injury			
subjects affected / exposed	0 / 249 (0.00%)	0 / 246 (0.00%)	1 / 249 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple injuries			
subjects affected / exposed	0 / 249 (0.00%)	0 / 246 (0.00%)	1 / 249 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skull fracture			

subjects affected / exposed	0 / 249 (0.00%)	1 / 246 (0.41%)	0 / 249 (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
Vascular disorders			
Kawasaki's disease			
subjects affected / exposed	1 / 249 (0.40%)	0 / 246 (0.00%)	0 / 249 (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			
Febrile convulsion			
subjects affected / exposed	0 / 249 (0.00%)	1 / 246 (0.41%)	0 / 249 (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			
Anaemia			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 249 (0.00%)	0 / 246 (0.00%)	1 / 249 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Milk allergy			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 249 (0.00%)	1 / 246 (0.41%)	0 / 249 (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
Respiratory, thoracic and mediastinal disorders			
Atelectasis			
subjects affected / exposed	0 / 249 (0.00%)	0 / 246 (0.00%)	1 / 249 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchospasm			
subjects affected / exposed	0 / 249 (0.00%)	1 / 246 (0.41%)	0 / 249 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Infections and infestations			
Bronchiolitis			
subjects affected / exposed	1 / 249 (0.40%)	4 / 246 (1.63%)	3 / 249 (1.20%)
occurrences causally related to treatment / all	0 / 1	0 / 5	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 249 (0.00%)	0 / 246 (0.00%)	1 / 249 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Exanthema subitum			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 249 (0.40%)	0 / 246 (0.00%)	0 / 249 (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	1 / 249 (0.40%)	0 / 246 (0.00%)	2 / 249 (0.80%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis viral			
subjects affected / exposed	0 / 249 (0.00%)	0 / 246 (0.00%)	1 / 249 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pertussis			
subjects affected / exposed	0 / 249 (0.00%)	1 / 246 (0.41%)	0 / 249 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 249 (0.00%)	1 / 246 (0.41%)	2 / 249 (0.80%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	1 / 249 (0.40%)	1 / 246 (0.41%)	3 / 249 (1.20%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pneumonia viral			
subjects affected / exposed	0 / 249 (0.00%)	0 / 246 (0.00%)	1 / 249 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	1 / 249 (0.40%)	0 / 246 (0.00%)	0 / 249 (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	1 / 249 (0.40%)	1 / 246 (0.41%)	0 / 249 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	1 / 249 (0.40%)	0 / 246 (0.00%)	0 / 249 (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

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

Non-serious adverse events	rMenB+ACWY Group	MenACWY Group	rMenB Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	240 / 249 (96.39%)	221 / 246 (89.84%)	232 / 249 (93.17%)
Nervous system disorders			
Somnolence			
subjects affected / exposed	106 / 249 (42.57%)	87 / 246 (35.37%)	115 / 249 (46.18%)
occurrences (all)	226	189	236
General disorders and administration site conditions			
Injection site pain			
subjects affected / exposed	212 / 249 (85.14%)	131 / 246 (53.25%)	207 / 249 (83.13%)
occurrences (all)	593	267	583
Crying			
subjects affected / exposed	176 / 249 (70.68%)	129 / 246 (52.44%)	184 / 249 (73.90%)
occurrences (all)	434	301	463
Injection site erythema			

subjects affected / exposed	147 / 249 (59.04%)	104 / 246 (42.28%)	162 / 249 (65.06%)
occurrences (all)	424	211	480
Injection site induration			
subjects affected / exposed	144 / 249 (57.83%)	57 / 246 (23.17%)	152 / 249 (61.04%)
occurrences (all)	575	116	609
Injection site swelling			
subjects affected / exposed	130 / 249 (52.21%)	56 / 246 (22.76%)	138 / 249 (55.42%)
occurrences (all)	380	88	403
Pyrexia			
subjects affected / exposed	125 / 249 (50.20%)	60 / 246 (24.39%)	121 / 249 (48.59%)
occurrences (all)	201	79	210
Gastrointestinal disorders			
Diarrhoea			
alternative assessment type: Non-systematic			
subjects affected / exposed	108 / 249 (43.37%)	89 / 246 (36.18%)	98 / 249 (39.36%)
occurrences (all)	181	163	196
Vomiting			
alternative assessment type: Non-systematic			
subjects affected / exposed	36 / 249 (14.46%)	49 / 246 (19.92%)	64 / 249 (25.70%)
occurrences (all)	51	82	105
Respiratory, thoracic and mediastinal disorders			
Bronchial hyperreactivity			
alternative assessment type: Non-systematic			
subjects affected / exposed	17 / 249 (6.83%)	15 / 246 (6.10%)	12 / 249 (4.82%)
occurrences (all)	25	26	16
Bronchospasm			
alternative assessment type: Non-systematic			
subjects affected / exposed	9 / 249 (3.61%)	13 / 246 (5.28%)	12 / 249 (4.82%)
occurrences (all)	13	23	16
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	46 / 249 (18.47%)	42 / 246 (17.07%)	57 / 249 (22.89%)
occurrences (all)	62	62	81
Dermatitis diaper			

subjects affected / exposed	12 / 249 (4.82%)	14 / 246 (5.69%)	16 / 249 (6.43%)
occurrences (all)	16	15	16
Dermatitis atopic			
subjects affected / exposed	6 / 249 (2.41%)	17 / 246 (6.91%)	11 / 249 (4.42%)
occurrences (all)	6	20	12
Psychiatric disorders			
Irritability			
alternative assessment type: Non-systematic			
subjects affected / exposed	155 / 249 (62.25%)	125 / 246 (50.81%)	170 / 249 (68.27%)
occurrences (all)	409	320	418
Eating disorder			
alternative assessment type: Non-systematic			
subjects affected / exposed	110 / 249 (44.18%)	85 / 246 (34.55%)	100 / 249 (40.16%)
occurrences (all)	214	162	194
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	81 / 249 (32.53%)	78 / 246 (31.71%)	87 / 249 (34.94%)
occurrences (all)	161	135	164
Viral upper respiratory tract infection			
subjects affected / exposed	72 / 249 (28.92%)	86 / 246 (34.96%)	82 / 249 (32.93%)
occurrences (all)	104	123	127
Pharyngitis			
subjects affected / exposed	50 / 249 (20.08%)	50 / 246 (20.33%)	50 / 249 (20.08%)
occurrences (all)	57	60	59
Bronchiolitis			
subjects affected / exposed	34 / 249 (13.65%)	37 / 246 (15.04%)	34 / 249 (13.65%)
occurrences (all)	40	37	37
Gastroenteritis			
subjects affected / exposed	31 / 249 (12.45%)	38 / 246 (15.45%)	40 / 249 (16.06%)
occurrences (all)	37	43	44
Conjunctivitis			
subjects affected / exposed	20 / 249 (8.03%)	24 / 246 (9.76%)	18 / 249 (7.23%)
occurrences (all)	23	25	18
Candida nappy rash			
subjects affected / exposed	15 / 249 (6.02%)	6 / 246 (2.44%)	12 / 249 (4.82%)
occurrences (all)	16	6	14

Rhinitis			
subjects affected / exposed	14 / 249 (5.62%)	19 / 246 (7.72%)	13 / 249 (5.22%)
occurrences (all)	17	21	16
Viral rash			
subjects affected / exposed	13 / 249 (5.22%)	13 / 246 (5.28%)	14 / 249 (5.62%)
occurrences (all)	13	13	14

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported