



Clinical trial results:

A Phase IV, Open-Label, Multi-Center Study to Evaluate the Safety and the 1-year Persistence of Antibody Response Among Children Who Received 4 Doses of the GSK MenACWY Conjugate Vaccine at 2, 4, 6 and 12 Months of Age in South Korea.

Summary

EudraCT number	2014-005392-90
Trial protocol	Outside EU/EEA
Global end of trial date	05 July 2018

Results information

Result version number	v1 (current)
This version publication date	31 December 2018
First version publication date	31 December 2018

Trial information

Trial identification

Sponsor protocol code	205336
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02446691
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline
Sponsor organisation address	Rue de l'Institut 89, Rixensart, Belgium,
Public contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089-904466, sss42438@gsk.com
Scientific contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089-904466, sss42438@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?	
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	29 August 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 December 2017
Global end of trial reached?	Yes
Global end of trial date	05 July 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

1. To evaluate the persistence of the antibody response against N. meningitidis serogroups A, C, W and Y at approximately 1 year after completion of a 4-dose infant vaccination series (2, 4, 6 and 12 months of age) of MenACWY vaccine as measured by hSBA titers ≥ 8 .
2. To evaluate the persistence of the antibody response against N. meningitidis serogroups A, C, W and Y at approximately 1 year after completion of a 4-dose infant vaccination series (2, 4, 6 and 12 months of age) of MenACWY vaccine as measured by rSBA titers ≥ 8 and ≥ 128 .

Protection of trial subjects:

All subjects were supervised/observed for 30 minutes after vaccination with appropriate medical treatment readily available. Vaccines were administered by qualified and trained personnel. Vaccines were administered only to eligible subjects that had no contraindications to any components of the vaccines/products.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 July 2015
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	Korea, Republic of: 128
Worldwide total number of subjects	128
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)	128
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:

Subjects were enrolled from 6 centers in South Korea.

Pre-assignment

Screening details:

All enrolled subjects were vaccinated

Period 1

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

Blinding implementation details:

This was an open label study. No blinding methods were used.

Arms

Arm title	MenACWY Group
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Arm description:

Healthy male and female infants approximately 2 months (55-89 days) of age on the day of consent, who received 4 doses of the GSK MenACWY Conjugate Vaccine, administered intramuscularly, at 2, 4, 6 and 12 months of age.

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

Dosage and administration details:

Infants received 4 doses of the Meningococcal Vaccine intramuscularly.

Number of subjects in period 1	MenACWY Group
Started	128
Completed	117
Not completed	11
Consent withdrawn by subject	2
Lost to follow-up	8
Protocol deviation	1

Baseline characteristics

Reporting groups

Reporting group title	MenACWY Group
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Reporting group description:

Healthy male and female infants approximately 2 months (55-89 days) of age on the day of consent, who received 4 doses of the GSK MenACWY Conjugate Vaccine, administered intramuscularly, at 2, 4, 6 and 12 months of age.

Reporting group values	MenACWY Group	Total	
Number of subjects	128	128	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	128	128	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Age Continuous			
Units: Days			
arithmetic mean	71.7		
standard deviation	± 8.09	-	
Sex: Female, Male			
Units: Subjects			
Female	59	59	
Male	69	69	
Race/Ethnicity, Customized			
Units: Subjects			
Asian	127	127	
Unspecified	1	1	

End points

End points reporting groups

Reporting group title	MenACWY Group
Reporting group description:	
Healthy male and female infants approximately 2 months (55-89 days) of age on the day of consent, who received 4 doses of the GSK MenACWY Conjugate Vaccine, administered intramuscularly, at 2, 4, 6 and 12 months of age.	

Primary: Number of subjects with any solicited Adverse Events (AEs) within 30 minutes after each vaccination.

End point title	Number of subjects with any solicited Adverse Events (AEs) within 30 minutes after each vaccination. ^[1]
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End point description:

Solicited signs and symptoms occurring within 30 minutes following each vaccination, include solicited local events (e.g. injection site erythema, induration and tenderness -threshold for Erythema and Induration: Type II- None [$<10\text{mm}$], Any [$\geq 10\text{ mm}$]), solicited systemic events (e.g. change in eating habits, sleepiness, irritability, vomiting, diarrhea, fever[body temperature $\geq 38^{\circ}\text{C}$ measured preferably via tympanic route]), and any other solicited event like use of analgesic/antipyretics for treatment or for prophylaxis. Analysis was performed on the solicited safety set, which included all subjects who received a study vaccination and reported any solicited adverse event data and/or indicators of solicited adverse events.

End point type	Primary
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End point timeframe:

Within 30 minutes of each vaccination

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The scope of this endpoint was descriptive analysis. No statistical analyses were performed.

End point values	MenACWY Group			
Subject group type	Reporting group			
Number of subjects analysed	128			
Units: Participants				
Injection site erythema,Vaccination 1,Any	0			
Injection site erythema,Vaccination 2,Any	0			
Injection site erythema, Vaccination 3,Any	0			
Injection site erythema,Vaccination 4,Any(N-124)	1			
Injection site induration,Vaccination 1, Any	0			
Injection site induration,Vaccination 2, Any	0			
Injection site induration,Vaccination 3, Any	0			
Injection site induration,Vaccination 4,Any(N-124)	1			
Injection site tenderness,Vaccination 1, Any	0			
Injection site tenderness,Vaccination 2, Any	0			

Injection site tenderness,Vaccination 3, Any	0			
Injection site tenderness,Vaccination 4,Any(N-124)	0			
Change in eating habits,Vaccination 1,Any	0			
Change in eating habits,Vaccination 2,Any	0			
Change in eating habits,Vaccination 3,Any	0			
Change in eating habits,Vaccination 4,Any(N-124)	0			
Diarrhea, Vaccination 1, Any	0			
Diarrhea, Vaccination 2, Any	0			
Diarrhea, Vaccination 3, Any	0			
Diarrhea,Vaccination 4,Any (N-124)	0			
Irritability, Vaccination 1, Any	0			
Irritability, Vaccination 2, Any	0			
Irritability, Vaccination 3, Any	0			
Irritability,Vaccination 4,Any(N-124)	0			
Sleepiness, Vaccination 1, Any	0			
Sleepiness, Vaccination 2, Any	0			
Sleepiness, Vaccination 3, Any	0			
Sleepiness,Vaccination 4,Any(N-124)	0			
Vomiting, Vaccination 1, Any	0			
Vomiting, Vaccination 2, Any	0			
Vomiting, Vaccination 3, Any	0			
Vomiting,Vaccination 4,Any(N-124)	1			
Fever, Vaccination 1, Yes	0			
Fever, Vaccination 1, No	128			
Fever, Vaccination 2, Yes	0			
Fever, Vaccination 2, No	128			
Fever, Vaccination 3, Yes	0			
Fever, Vaccination 3, No	128			
Fever, Vaccination 4, Yes	0			
Fever, Vaccination 4, No(N-124)	124			

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with any solicited local AEs from Day 1 to Day 7 after each vaccination

End point title	Number of subjects with any solicited local AEs from Day 1 to Day 7 after each vaccination ^[2]
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End point description:

Solicited local AEs reported from day 1 to day 7 after each vaccination were assessed. Assessed local symptoms include injection site erythema, injection site induration and injection site tenderness. Any = incidence of a particular symptom regardless of intensity grade.Threshold for Erythema and Induration:Type II None (<10 mm), Any (>=10 mm).Analysis was performed on the solicited safety set, which included all subjects who received a study vaccination and reported any solicited adverse event data and/or indicators of solicited adverse events.

End point type	Primary
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End point timeframe:

From Day 1 to Day 7 after each vaccination

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The scope of this endpoint was descriptive analysis. No statistical analyses were performed.

End point values	MenACWY Group			
Subject group type	Reporting group			
Number of subjects analysed	128			
Units: Participants				
Injection site erythema, Vaccination 1, Any	4			
Injection site erythema, Vaccination 2, Any	6			
Injection site erythema,Vaccination 3, Any(N-127)	6			
Injection site erythema,Vaccination 4, Any(N-124)	6			
Injection site induration,Vaccination 1,Any	4			
Injection site induration,Vaccination 2,Any	9			
Injection site induration,Vaccination 3,Any(N-127)	3			
Injection site induration,Vaccination 4,Any(N-124)	6			
Injection site tenderness,Vaccination 1,Any	17			
Injection site tenderness,Vaccination 2,Any	21			
Injection site tenderness,Vaccination 3,Any(N-127)	14			
Injection site tenderness,Vaccination 4,Any(N-124)	20			

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with any solicited systemic AEs from Day 1 to Day 7 after each vaccination.

End point title	Number of subjects with any solicited systemic AEs from Day 1 to Day 7 after each vaccination. ^[3]
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End point description:

Solicited systemic AEs reported from day 1 to day 7 after each vaccination were assessed. Assessed systemic symptoms include change in eating habits, sleepiness, irritability, vomiting, diarrhea and fever (body temperature $\geq 38^{\circ}\text{C}$ (100.4°F)). Analysis was performed on the solicited safety set, which included all subjects who received a study vaccination and reported any solicited adverse event data and/or indicators of solicited adverse events.

End point type	Primary
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End point timeframe:

From Day 1 to Day 7 after each vaccination

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The scope of this endpoint was descriptive analysis. No statistical analyses were performed.

End point values	MenACWY Group			
Subject group type	Reporting group			
Number of subjects analysed	128			
Units: Participants				
Change in eating habits,Vaccination 1,Any	29			
Change in eating habits,Vaccination 2,Any	21			
Change in eating habits,Vaccination 3,Any(N-127)	21			
Change in eating habits,Vaccination 4,Any(N-124)	24			
Diarrhea,Vaccination 1,Any	15			
Diarrhea, Vaccination 2, Any	13			
Diarrhea, Vaccination 3, Any(N-127)	15			
Diarrhea, Vaccination 4, Any(N-124)	17			
Irritability, Vaccination 1, Any	58			
Irritability, Vaccination 2, Any	49			
Irritability,Vaccination 3,Any(N-127)	47			
Irritability,Vaccination 4,Any(N-124)	45			
Sleepiness,Vaccination 1,Any	52			
Sleepiness, Vaccination 2, Any	31			
Sleepiness,Vaccination 3,Any(N-127)	28			
Sleepiness,Vaccination 4,Any(N-124)	20			
Vomiting, Vaccination 1, Any	26			
Vomiting, Vaccination 2, Any	20			
Vomiting,Vaccination 3,Any(N-127)	15			
Vomiting,Vaccination 4,Any(N-124)	5			
Fever, Vaccination 1, Yes	4			
Fever, Vaccination 1, No	124			
Fever, Vaccination 2, Yes	10			
Fever, Vaccination 2, No	118			
Fever, Vaccination 3, Yes(N-127)	6			
Fever, Vaccination 3, No(N-127)	121			
Fever, Vaccination 4, Yes(N-124)	15			
Fever, Vaccination 4, No(N-124)	109			

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with any medically attended unsolicited AEs and AEs leading to premature withdrawal

End point title	Number of subjects with any medically attended unsolicited AEs and AEs leading to premature withdrawal ^[4]
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End point description:

An unsolicited adverse event is an adverse event that was not solicited using a Subject Diary and that was spontaneously communicated by a subject parent(s)/legal guardian(s)] who has signed the informed consent. All medically attended unsolicited AEs were collected from Day 1 to Visit 6. Analysis was performed on the unsolicited safety set, which included all subjects who received a study vaccination and reported any unsolicited adverse event data.

End point type	Primary
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End point timeframe:

From Day 1 to Visit 6 (at 24 Months of age)

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The scope of this endpoint was descriptive analysis. No statistical analyses were performed.

End point values	MenACWY Group			
Subject group type	Reporting group			
Number of subjects analysed	128			
Units: Participants				
Any Medically Attended Unsolicited AEs	85			
AEs leading to premature withdrawal	0			

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with Serious AEs (SAEs)

End point title	Number of subjects with Serious AEs (SAEs) ^[5]
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End point description:

Subjects reporting SAEs from day 1 to visit 6 (at 24 months of age) were assessed. A serious adverse event (SAE) is defined as any untoward medical occurrence that at any dose results in one or more of the following: death, is life-threatening, required or prolonged hospitalization, persistent or significant disability/incapacity, congenital anomaly/or birth defect, An important and significant medical event that may not be immediately life threatening or resulting in death or hospitalization but, based upon appropriate medical judgment, may jeopardize the subject or may require intervention to prevent one of the other outcomes listed above. Analysis was performed on the overall safety set, which included all subjects who received a study vaccination and reported any solicited/unsolicited adverse event data.

End point type	Primary
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End point timeframe:

From Day 1 to Visit 6 (At 24 months of age)

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The scope of this endpoint was descriptive analysis. No statistical analyses were performed.

End point values	MenACWY Group			
Subject group type	Reporting group			
Number of subjects analysed	128			
Units: Participants	26			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of subjects with human Serum Bactericidal Assay (hSBA) titers ≥ 8 against each N.meningitidis serogroup A,C,W and Y at 24 months of age.

End point title	Percentage of subjects with human Serum Bactericidal Assay (hSBA) titers ≥ 8 against each N.meningitidis serogroup A,C,W and Y at 24 months of age. ^[6]
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End point description:

To assess antibody persistence against N. meningitidis serogroups A, C, W and Y at 1 year after completion of a 4-dose infant vaccination series (2, 4, 6 and 12 months of age) of MenACWY vaccine as measured by serum bactericidal assay using human serum complement. Analysis was performed on the Full analysis set (FAS), which included all enrolled subjects who received at least one study vaccination and provided an evaluable hSBA Visit 6 assessment, one year after completion of a 4-dose infant vaccination series (2, 4, 6 and 12 months of age), for at least one serogroup.

End point type	Primary
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End point timeframe:

At 24 months of age (Visit 6)

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The scope of this endpoint was descriptive analysis. No statistical analyses were performed.

End point values	MenACWY Group			
Subject group type	Reporting group			
Number of subjects analysed	114			
Units: Percentage of subjects				
number (confidence interval 95%)				
Serogroup A	39 (30.4 to 49.1)			
Serogroup C (N-110)	61 (51.1 to 70.1)			
Serogroup W (N-113)	88 (80.1 to 93.1)			
Serogroup Y	89 (81.3 to 93.8)			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of subjects with rabbit Serum Bactericidal Assay (rSBA) titers ≥ 8 , against each N.meningitidis serogroup at 24 months of age

End point title	Percentage of subjects with rabbit Serum Bactericidal Assay (rSBA) titers ≥ 8 , against each N.meningitidis serogroup at 24
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End point description:

To assess antibody persistence against N. Meningitidis serogroups A, C, W and Y at 1 year after completion of a 4-dose infant vaccination series (2, 4, 6 and 12 months of age) of MenACWY vaccine as measured by serum bactericidal assay using rabbit serum complement. Analysis was performed on the FAS, which included all enrolled subjects who receive at least one study vaccination and provided an evaluable rSBA Visit 6 assessment, one year after completion of a 4-dose infant vaccination series (2, 4, 6 and 12 months of age), for at least one serogroup.

End point type

Primary

End point timeframe:

At 24 months of age (Visit 6)

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The scope of this endpoint was descriptive analysis. No statistical analyses were performed.

End point values	MenACWY Group			
Subject group type	Reporting group			
Number of subjects analysed	108			
Units: Percentage of subjects				
number (confidence interval 95%)				
Serogroup A	99 (94.9 to 99.98)			
Serogroup C	54 (43.8 to 63.3)			
Serogroup W	69 (59.8 to 77.9)			
Serogroup Y(N-107)	90 (82.3 to 94.8)			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of subjects with rabbit Serum Bactericidal Assay (rSBA) titers ≥ 128 against each N.meningitidis serogroup at 24 months of age

End point title

Percentage of subjects with rabbit Serum Bactericidal Assay (rSBA) titers ≥ 128 against each N.meningitidis serogroup at 24 months of age^[8]

End point description:

To assess antibody persistence against N. Meningitidis serogroups A, C, W and Y at 1 year after completion of a 4-dose infant vaccination series (2, 4, 6 and 12 months of age) of MenACWY vaccine as measured by serum bactericidal assay using rabbit serum complement. Analysis was performed on the FAS, which included all enrolled subjects who receive at least one study vaccination and provided an evaluable rSBA Visit 6 assessment, one year after completion of a 4-dose infant vaccination series (2, 4, 6 and 12 months of age), for at least one serogroup.

End point type

Primary

End point timeframe:

At 24 months of age (Visit 6)

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The scope of this endpoint was descriptive analysis. No statistical analyses were performed.

End point values	MenACWY Group			
Subject group type	Reporting group			
Number of subjects analysed	108			
Units: Percentage of subjects				
number (confidence interval 95%)				
Serogroup A	98 (93.5 to 99.77)			
Serogroup C	30 (21.2 to 39.2)			
Serogroup W	62 (52.2 to 71.2)			
Serogroup Y(N-107)	80 (71.6 to 87.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with hSBA ≥ 8 against each N. meningitidis serogroups A, C, W and Y at 13 months of age

End point title	Percentage of Subjects with hSBA ≥ 8 against each N. meningitidis serogroups A, C, W and Y at 13 months of age
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End point description:

To assess antibody response against N. meningitidis serogroups A, C, W and Y at 1 month after completion of a 4-dose infant vaccination series (2, 4, 6 and 12 months of age) of MenACWY vaccine as measured by serum bactericidal assay using human serum complement. The Analysis was done on FAS hSBA 1 month, which included all enrolled subjects who received at least one study vaccination and who provided evaluable hSBA immunogenicity data at 1 month after last vaccination for at least one serogroup.

End point type	Secondary
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End point timeframe:

At 13 months of age (Visit 5)

End point values	MenACWY Group			
Subject group type	Reporting group			
Number of subjects analysed	122			
Units: Percentage of subjects				
number (confidence interval 95%)				
Serogroup A	94 (88.5 to 97.7)			
Serogroup C	98 (94.2 to 99.80)			
Serogroup W	100 (97.0 to 100.0)			
Serogroup Y(N-120)	100 (97.0 to 100.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with rSBA titers ≥ 8 against each N. meningitidis serogroups A, C, W and Y at 13 months of age

End point title	Percentage of Subjects with rSBA titers ≥ 8 against each N. meningitidis serogroups A, C, W and Y at 13 months of age
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End point description:

To assess antibody response against N. meningitidis serogroups A, C, W and Y at 1 month after completion of a 4-dose infant vaccination series (2, 4, 6 and 12 months of age) of MenACWY vaccine as measured by serum bactericidal assay using rabbit serum complement. The Analysis was done on FAS rSBA 1 month, which included all enrolled subjects who received at least one study vaccination and who provided evaluable rSBA immunogenicity data at 1 month after last vaccination for at least one serogroup.

End point type	Secondary
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End point timeframe:

At 13 months of age (Visit 5)

End point values	MenACWY Group			
Subject group type	Reporting group			
Number of subjects analysed	116			
Units: Percentage of subjects				
number (confidence interval 95%)				
Serogroup A (N-115)	100 (96.8 to 100.0)			
Serogroup C(N-115)	99 (95.3 to 99.98)			
Serogroup W(N-115)	100 (96.8 to 100.0)			
Serogroup Y	100 (96.9 to 100.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with rSBA titers ≥ 128 against each N. meningitidis serogroups A, C, W and Y at 13 months of age

End point title	Percentage of Subjects with rSBA titers ≥ 128 against each N. meningitidis serogroups A, C, W and Y at 13 months of age
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End point description:

To assess antibody response against N. meningitidis serogroups A, C, W and Y at 1 month after completion of a 4-dose infant vaccination series (2, 4, 6 and 12 months of age) of MenACWY vaccine as measured by serum bactericidal assay using rabbit serum complement. The Analysis was done on FAS rSBA 1 month, which included all enrolled subjects who received at least one study vaccination and who provided evaluable rSBA immunogenicity data at 1 month after last vaccination for at least one serogroup.

End point type	Secondary
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End point timeframe:

At 13 months of age (Visit 5)

End point values	MenACWY Group			
Subject group type	Reporting group			
Number of subjects analysed	116			
Units: Percentage of subjects				
number (confidence interval 95%)				
Serogroup A(N-115)	100 (96.8 to 100.0)			
Serogroup C(N-115)	92 (85.7 to 96.4)			
Serogroup W(N-115)	98 (93.9 to 99.79)			
Serogroup Y	98 (93.9 to 99.79)			

Statistical analyses

No statistical analyses for this end point

Secondary: hSBA Geometric Mean Titers (GMTs) against each N. meningitidis serogroups A, C, W and Y at 24 months of age

End point title	hSBA Geometric Mean Titers (GMTs) against each N. meningitidis serogroups A, C, W and Y at 24 months of age
End point description:	
To assess persistence of antibody response in terms of GMTs using hSBA assay against N. meningitidis serogroups A, C, W and Y at 1 year after completion of a 4-dose infant vaccination series (2, 4, 6 and 12 months of age) of MenACWY vaccine. Analysis was performed on the Full analysis set (FAS), which included all enrolled subjects who received atleast one study vaccination and provided an evaluable hSBA Visit 6 assessment, one year after completion of a 4-dose infant vaccination series (2, 4, 6 and 12 months of age), for atleast one serogroup.	
End point type	Secondary
End point timeframe:	
At 24 months of age (Visit 6)	

End point values	MenACWY Group			
Subject group type	Reporting group			
Number of subjects analysed	114			
Units: Titers				
geometric mean (confidence interval 95%)				
Serogroup A	6.80 (5.19 to 8.93)			
Serogroup C(N-110)	13.04 (9.65 to 17.63)			
Serogroup W(N-113)	53.56 (40.42 to 70.97)			

Serogroup Y	50.75 (38.76 to 66.45)			
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Statistical analyses

No statistical analyses for this end point

Secondary: rSBA GMTs against each N. meningitidis serogroups A, C, W and Y at 24 months of age

End point title	rSBA GMTs against each N. meningitidis serogroups A, C, W and Y at 24 months of age
End point description: To assess persistence of antibody response in terms of GMTs using rSBA assay against N. meningitidis serogroups A, C, W and Y at 1 year after completion of a 4-dose infant vaccination series (2, 4, 6 and 12 months of age) of MenACWY vaccine. Analysis was performed on the Full analysis set (FAS), which included all enrolled subjects who received atleast one study vaccination and provided an evaluable rSBA Visit 6 assessment, one year after completion of a 4-dose infant vaccination series (2, 4, 6 and 12 months of age), for atleast one serogroup.	
End point type	Secondary
End point timeframe: At 24 months of age (Visit 6)	

End point values	MenACWY Group			
Subject group type	Reporting group			
Number of subjects analysed	108			
Units: Titers				
geometric mean (confidence interval 95%)				
Serogroup A	2269.48 (1761.12 to 2924.59)			
Serogroup C	17.17 (11.28 to 26.14)			
Serogroup W	114.04 (65.22 to 199.39)			
Serogroup Y(N-107)	310.91 (203.23 to 475.65)			

Statistical analyses

No statistical analyses for this end point

Secondary: hSBA GMTs against each N. meningitidis serogroups A, C, W and Y at 13 months of age

End point title	hSBA GMTs against each N. meningitidis serogroups A, C, W and Y at 13 months of age
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End point description:

To assess antibody response in terms of GMTs using hSBA assay against N. meningitidis serogroups A, C, W and Y at 1 month after completion of a 4-dose infant vaccination series (2, 4, 6 and 12 months of age) of MenACWY vaccine. The Analysis was done on FAS hSBA 1 month, which included all enrolled subjects who received at least one study vaccination and provided evaluable hSBA immunogenicity data at 1 month after last vaccination for at least one serogroup.

End point type	Secondary
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End point timeframe:

At 13 months of age (Visit 5)

End point values	MenACWY Group			
Subject group type	Reporting group			
Number of subjects analysed	122			
Units: Titers				
geometric mean (confidence interval 95%)				
Serogroup A	107.90 (85.73 to 135.81)			
Serogroup C	201.04 (157.90 to 255.96)			
Serogroup W	426.74 (338.34 to 538.24)			
Serogroup Y(N-120)	359.39 (280.59 to 460.31)			

Statistical analyses

No statistical analyses for this end point

Secondary: rSBA GMTs against each N. meningitidis serogroups A, C, W and Y at 13 months of age.

End point title	rSBA GMTs against each N. meningitidis serogroups A, C, W and Y at 13 months of age.
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End point description:

To assess antibody response in terms of GMTs using rSBA assay against N. meningitidis serogroups A, C, W and Y at 1 month after completion of a 4-dose infant vaccination series (2, 4, 6 and 12 months of age) of MenACWY vaccine. The Analysis was done on FAS rSBA 1 month, which included all enrolled subjects who received at least one study vaccination and provided evaluable rSBA immunogenicity data at 1 month after last vaccination for at least one serogroup.

End point type	Secondary
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End point timeframe:

At 13 months of age (Visit 5)

End point values	MenACWY Group			
Subject group type	Reporting group			
Number of subjects analysed	116			
Units: Titers				
geometric mean (confidence interval 95%)				
Serogroup A(N-115)	7394.18 (6057.42 to 9025.93)			
Serogroup C(N-115)	735.07 (545.22 to 991.03)			
Serogroup W(N-115)	2718.69 (2031.77 to 3637.85)			
Serogroup Y	2226.70 (1731.21 to 2863.99)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited local and systemic adverse events (AEs): from Day 1 to Day 7 after each vaccination.

Unsolicited AEs, Serious AEs (SAEs): From Day 1 to study end (visit 6).

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	21.0
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Reporting groups

Reporting group title	MenACWY Group
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Reporting group description:

Healthy male and female infants approximately 2 months (55-89 days) of age on the day of consent, who received 4 doses of the GSK MenACWY Conjugate Vaccine, administered intramuscularly, at 2, 4, 6 and 12 months of age.

Serious adverse events	MenACWY Group		
Total subjects affected by serious adverse events			
subjects affected / exposed	26 / 128 (20.31%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cholesteatoma			
subjects affected / exposed	1 / 128 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Ligament rupture			
subjects affected / exposed	1 / 128 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tendon injury			
subjects affected / exposed	1 / 128 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Contusion			

subjects affected / exposed	1 / 128 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Congenital, familial and genetic disorders			
Buried penis syndrome			
subjects affected / exposed	1 / 128 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Seizure			
subjects affected / exposed	1 / 128 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Enteritis			
subjects affected / exposed	1 / 128 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Bronchiolitis			
subjects affected / exposed	5 / 128 (3.91%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 0		
Croup infectious			
subjects affected / exposed	1 / 128 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			
subjects affected / exposed	1 / 128 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hand-foot-and-mouth disease			

subjects affected / exposed	1 / 128 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Herpangina			
subjects affected / exposed	1 / 128 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pharyngitis			
subjects affected / exposed	1 / 128 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pharyngotonsillitis			
subjects affected / exposed	1 / 128 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	4 / 128 (3.13%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Pneumonia influenzal			
subjects affected / exposed	1 / 128 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia parainfluenzae viral			
subjects affected / exposed	1 / 128 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia respiratory syncytial viral			
subjects affected / exposed	1 / 128 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia viral			

subjects affected / exposed	1 / 128 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tonsillitis			
subjects affected / exposed	2 / 128 (1.56%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Upper respiratory tract infection			
subjects affected / exposed	2 / 128 (1.56%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	3 / 128 (2.34%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Viral infection			
subjects affected / exposed	1 / 128 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	MenACWY Group		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	112 / 128 (87.50%)		
General disorders and administration site conditions			
Injection site pain			
subjects affected / exposed	41 / 128 (32.03%)		
occurrences (all)	136		
Pyrexia			
subjects affected / exposed	33 / 128 (25.78%)		
occurrences (all)	68		
Injection site induration			

subjects affected / exposed occurrences (all) 22 / 128 (17.19%) 67			
Injection site erythema subjects affected / exposed occurrences (all) 16 / 128 (12.50%) 40			
Immune system disorders Atopy subjects affected / exposed occurrences (all) 1 / 128 (0.78%) 1 Hypersensitivity subjects affected / exposed occurrences (all) 1 / 128 (0.78%) 1			
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) 6 / 128 (4.69%) 7 Rhinorrhoea subjects affected / exposed occurrences (all) 4 / 128 (3.13%) 9			
Psychiatric disorders Irritability subjects affected / exposed occurrences (all) 86 / 128 (67.19%) 461			
Injury, poisoning and procedural complications Concussion subjects affected / exposed occurrences (all) 4 / 128 (3.13%) 4 Contusion subjects affected / exposed occurrences (all) 1 / 128 (0.78%) 1 Ear canal injury subjects affected / exposed occurrences (all) 1 / 128 (0.78%) 1 Eye contusion subjects affected / exposed occurrences (all) 1 / 128 (0.78%) 1			

Foreign body in gastrointestinal tract subjects affected / exposed occurrences (all)	1 / 128 (0.78%) 1		
Hand fracture subjects affected / exposed occurrences (all)	1 / 128 (0.78%) 1		
Head injury subjects affected / exposed occurrences (all)	1 / 128 (0.78%) 1		
Lip injury subjects affected / exposed occurrences (all)	2 / 128 (1.56%) 2		
Radial head dislocation subjects affected / exposed occurrences (all)	1 / 128 (0.78%) 2		
Skin abrasion subjects affected / exposed occurrences (all)	1 / 128 (0.78%) 1		
Skull fracture subjects affected / exposed occurrences (all)	1 / 128 (0.78%) 1		
Thermal burn subjects affected / exposed occurrences (all)	1 / 128 (0.78%) 1		
Congenital, familial and genetic disorders Hydrocele subjects affected / exposed occurrences (all)	1 / 128 (0.78%) 1		
Nervous system disorders Somnolence subjects affected / exposed occurrences (all)	67 / 128 (52.34%) 265		
Ear and labyrinth disorders Tympanic membrane perforation subjects affected / exposed occurrences (all)	1 / 128 (0.78%) 1		

Eye disorders			
Eye discharge			
subjects affected / exposed	2 / 128 (1.56%)		
occurrences (all)	2		
Retinal disorder			
subjects affected / exposed	1 / 128 (0.78%)		
occurrences (all)	1		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 128 (0.78%)		
occurrences (all)	1		
Diarrhoea			
subjects affected / exposed	41 / 128 (32.03%)		
occurrences (all)	178		
Enteritis			
subjects affected / exposed	1 / 128 (0.78%)		
occurrences (all)	1		
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 128 (0.78%)		
occurrences (all)	1		
Haematochezia			
subjects affected / exposed	2 / 128 (1.56%)		
occurrences (all)	2		
Mouth ulceration			
subjects affected / exposed	1 / 128 (0.78%)		
occurrences (all)	1		
Stomatitis			
subjects affected / exposed	1 / 128 (0.78%)		
occurrences (all)	2		
Vomiting			
subjects affected / exposed	42 / 128 (32.81%)		
occurrences (all)	168		
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	1 / 128 (0.78%)		
occurrences (all)	1		
Dermatitis atopic			

subjects affected / exposed	1 / 128 (0.78%)		
occurrences (all)	1		
Dermatitis contact			
subjects affected / exposed	3 / 128 (2.34%)		
occurrences (all)	3		
Dry skin			
subjects affected / exposed	1 / 128 (0.78%)		
occurrences (all)	1		
Eczema			
subjects affected / exposed	4 / 128 (3.13%)		
occurrences (all)	4		
Pityriasis alba			
subjects affected / exposed	1 / 128 (0.78%)		
occurrences (all)	1		
Rash			
subjects affected / exposed	3 / 128 (2.34%)		
occurrences (all)	3		
Urticaria			
subjects affected / exposed	3 / 128 (2.34%)		
occurrences (all)	4		
Renal and urinary disorders			
Hydronephrosis			
subjects affected / exposed	1 / 128 (0.78%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	1 / 128 (0.78%)		
occurrences (all)	1		
Infections and infestations			
Adenovirus infection			
subjects affected / exposed	1 / 128 (0.78%)		
occurrences (all)	1		
Bronchiolitis			
subjects affected / exposed	11 / 128 (8.59%)		
occurrences (all)	14		
Bronchitis			

subjects affected / exposed	11 / 128 (8.59%)		
occurrences (all)	21		
Cellulitis			
subjects affected / exposed	1 / 128 (0.78%)		
occurrences (all)	1		
Croup infectious			
subjects affected / exposed	3 / 128 (2.34%)		
occurrences (all)	3		
Ear infection			
subjects affected / exposed	1 / 128 (0.78%)		
occurrences (all)	1		
Enterovirus infection			
subjects affected / exposed	3 / 128 (2.34%)		
occurrences (all)	4		
Exanthema subitum			
subjects affected / exposed	3 / 128 (2.34%)		
occurrences (all)	3		
Gastroenteritis			
subjects affected / exposed	9 / 128 (7.03%)		
occurrences (all)	10		
Gastroenteritis viral			
subjects affected / exposed	1 / 128 (0.78%)		
occurrences (all)	1		
Gianotti-Crosti syndrome			
subjects affected / exposed	1 / 128 (0.78%)		
occurrences (all)	1		
Hand-foot-and-mouth disease			
subjects affected / exposed	6 / 128 (4.69%)		
occurrences (all)	6		
Herpangina			
subjects affected / exposed	1 / 128 (0.78%)		
occurrences (all)	1		
Hordeolum			
subjects affected / exposed	1 / 128 (0.78%)		
occurrences (all)	1		
Impetigo			

subjects affected / exposed	1 / 128 (0.78%)		
occurrences (all)	1		
Nasopharyngitis			
subjects affected / exposed	15 / 128 (11.72%)		
occurrences (all)	18		
Oral candidiasis			
subjects affected / exposed	1 / 128 (0.78%)		
occurrences (all)	1		
Otitis externa			
subjects affected / exposed	1 / 128 (0.78%)		
occurrences (all)	1		
Otitis media			
subjects affected / exposed	5 / 128 (3.91%)		
occurrences (all)	5		
Otitis media acute			
subjects affected / exposed	11 / 128 (8.59%)		
occurrences (all)	13		
Parainfluenzae virus infection			
subjects affected / exposed	1 / 128 (0.78%)		
occurrences (all)	1		
Pharyngitis			
subjects affected / exposed	3 / 128 (2.34%)		
occurrences (all)	3		
Pharyngotonsillitis			
subjects affected / exposed	6 / 128 (4.69%)		
occurrences (all)	6		
Pneumonia			
subjects affected / exposed	5 / 128 (3.91%)		
occurrences (all)	7		
Respiratory tract infection viral			
subjects affected / exposed	1 / 128 (0.78%)		
occurrences (all)	1		
Rhinitis			
subjects affected / exposed	6 / 128 (4.69%)		
occurrences (all)	7		
Sinusitis			

subjects affected / exposed	2 / 128 (1.56%)		
occurrences (all)	3		
Tonsillitis			
subjects affected / exposed	1 / 128 (0.78%)		
occurrences (all)	1		
Upper respiratory tract infection			
subjects affected / exposed	32 / 128 (25.00%)		
occurrences (all)	52		
Viral infection			
subjects affected / exposed	4 / 128 (3.13%)		
occurrences (all)	4		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	2 / 128 (1.56%)		
occurrences (all)	2		
Hypophagia			
subjects affected / exposed	59 / 128 (46.09%)		
occurrences (all)	230		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 August 2015	Due to change in Market Authorization Holder from Novartis to GSK Vaccines, the protocol was revised to change name of sponsor

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported