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

Summary

EudraCT number	2015-001030-16
Trial protocol	Outside EU/EEA
Global end of trial date	11 February 2016

Results information

Result version number	v1
This version publication date	24 June 2016
First version publication date	24 June 2016

Trial information

Trial identification

Sponsor protocol code	V102_16E1

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline Biologicals
Sponsor organisation address	Rue de l'Institut 89, Rixensart, Belgium, B-1330
Public contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 44 2089904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 44 2089904466, GSKClinicalSupportHD@gsk.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Interim
Date of interim/final analysis	16 May 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	11 February 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

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

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 December 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 189
Worldwide total number of subjects	189
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	81

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

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

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

Period 1

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

Blinding implementation details:

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

Arms

Are arms mutually exclusive?	Yes
Arm title	MenABCWY

Arm description:

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

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

Dosage and administration details:

1 dose of 0.5 millilitres

Arm title	MenACWY

Arm description:

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

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

Dosage and administration details:

1 dose of 0.5 millilitres

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

Baseline characteristics

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

Reporting group values	MenABCWY	MenACWY	Total
Number of subjects	95	94	189
Age categorical			
Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			0
Newborns (0-27 days)			0
Infants and toddlers (28 days-23 months)			0
Children (2-11 years)			0
Adolescents (12-17 years)			0
Adults (18-64 years)			0
From 65-84 years			0
85 years and over			0
Age continuous			
Units: years			
arithmetic mean	12.8	12.4	
standard deviation	± 2.36	± 2.4	-
Gender categorical			
Units: Subjects			
Female	40	33	73
Male	55	61	116

End points

End points reporting groups

Reporting group title	MenABCWY

Reporting group description:

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

Reporting group title	MenACWY

Reporting group description:

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

Subject analysis set title	All Enrolled Set
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All screened subjects who provide informed consent and provide demographic and/or baseline screening assessments, regardless of the subject's assignment and treatment status in the study and received a Subject ID.

Subject analysis set title	All Exposed Set
Subject analysis set type	Safety analysis

Subject analysis set description:

All screened subjects who provide informed consent and provide demographic and/or baseline screening assessments, regardless of the subject's assignment and treatment status in the study, received a Subject ID and a study vaccination.

Subject analysis set title	Safety Set (solicited AEs and other solicited reactions)
Subject analysis set type	Safety analysis

Subject analysis set description:

All screened subjects who provide informed consent and provide demographic and/or baseline screening assessments, regardless of the subject's assignment and treatment status in the study, received a Subject ID and a study vaccination, and provided post-vaccination reactogenicity data.
AE = Adverse event.

Subject analysis set title	Safety Set (unsolicited adverse events)
Subject analysis set type	Safety analysis

Subject analysis set description:

All screened subjects who provide informed consent and provide demographic and/or baseline screening assessments, regardless of the subject's assignment and treatment status in the study, received a Subject ID and a study vaccination, and have post-vaccination unsolicited adverse event records.

Subject analysis set title	Safety Set (overall)
Subject analysis set type	Safety analysis

Subject analysis set description:

All screened subjects who provide informed consent and provide demographic and/or baseline screening assessments, regardless of the subject's assignment and treatment status in the study, received a Subject ID and a study vaccination, and have either post-vaccination reactogenicity data or post-vaccination unsolicited adverse event records.

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

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

End point description:

The effectiveness of three doses of MenABCWY vaccine when compared to one dose of MenACWY vaccine against a panel of US N. meningitidis serogroup B invasive disease strains at 1 month after the 3-dose vaccination series was evaluated in terms of: the combined percentage of subjects without bactericidal activity at 1:4 dilution using the human Serum Bactericidal Assay (hSBA) against each strain in MenABCWY group and MenACWY group. The percentages of subjects will be averaged across all

strains.

End point type	Primary

End point timeframe:

Day 31, 1 month after the 3-dose vaccination series

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 primary end point was descriptive, no statistical hypothesis test was performed.

End point values	MenABCWY	MenACWY		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[2]	0[3]		
Units: Percentage				
number (not applicable)				

Notes:

[2] - Results are not available yet.

[3] - Results are not available yet.

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Number of subjects reporting any solicited local or systemic AEs from Day 1 (6 hours) to Day 7 after any meningococcal vaccination is reported.

End point type	Secondary

End point timeframe:

Day 1 (6 hours) to Day 7 after vaccination

End point values	MenABCWY	MenACWY		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	90	87		
Units: Subjects				
Any (Vacc.1, N=90,87)	62	25		
Any Local Reactions (Vacc.1, N=90,87)	60	15		
Any Systemic Reactions (Vacc.1, N=90,87)	27	15		
Induration (mm) (Vacc.1, N=88,87)	6	0		
Erythema (mm) (Vacc.1, N=87,86)	6	0		
Pain (Vacc.1, N=88,87)	59	15		
Nausea (Vacc.1, N=87,87)	5	5		
Fatigue (Vacc.1, N=87,87)	14	11		
Myalgia (Vacc.1, N=87,85)	13	3		
Arthralgia (Vacc.1, N=86,85)	9	0		
Headache (Vacc.1, N=88,87)	13	9		

Fever (Vacc.1, N=90,85)	0	1		
Chills (Vacc.1, N=88,87)	2	3		
Loss of appetite (Vacc.1, N=88,87)	3	3		
Prevention of pain/fever (Vacc.1, N=85,84)	0	0		
Treatment of pain/fever (Vacc.1, N=85,84)	12	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting unsolicited AEs after any vaccination.

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

End point description:

The number of subjects reporting unsolicited AEs after any vaccination is reported.

End point type	Secondary

End point timeframe:

Day 1 to Day 30 after any vaccination

End point values	MenABCWY	MenACWY		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	93	93		
Units: Subjects				
Any AEs	14	11		

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

The number of subjects reporting any SAEs, medically-attended AEs and AEs leading to premature withdrawal during the entire study period is reported.

End point type	Secondary

End point timeframe:

During the entire study period

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

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited AEs were collected from day 1 to day 7, Unsolicited AEs were collected from day 1 to day 30, SAEs, medically attended AEs and AEs leading to withdrawal are collected for the whole duration of the study.

Adverse event reporting additional description:

Data will be presented in terms of number of subjects reporting AEs.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups

Reporting group title	MenABCWY

Reporting group description:

Subjects who received 2 doses of MenABCWY vaccine in the parent study, now receive the 3rd dose of MenABCWY vaccine in the current study.

Reporting group title	MenACWY

Reporting group description:

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

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

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

Non-serious adverse events	MenABCWY	MenACWY	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	67 / 95 (70.53%)	42 / 94 (44.68%)	
Nervous system disorders			
Headache			
subjects affected / exposed[1]	14 / 93 (15.05%)	9 / 93 (9.68%)	
occurrences (all)	25	27	
General disorders and administration site conditions			

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

Notes:

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

symptom sheets completed.

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

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

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

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

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

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