Clinical trial results:
A phase II, observer-blinded, multi-center, controlled study to assess the safety and immunogenicity of one dose of GlaxoSmithKline (GSK) Biologicals' meningococcal serogroup ACWY tetanus toxoid conjugate vaccine (MenACWY-TT) versus one dose of Sanofi Pasteur's meningococcal serogroups A, C, W-135 and Y vaccine (Menactra) in healthy subjects aged 10 through 25 years.

Summary

EudraCT number	2012-001305-25
Trial protocol	Outside EU/EEA
Global end of trial date	29 July 2011

Results information

Result version number	v3 (current)
This version publication date	16 September 2018
First version publication date	29 July 2015
Version creation reason	• Correction of full data set Minor corrections of the full study results.

Trial information

Trial identification

Sponsor protocol code	114249

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01165242
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	12 January 2012
Is this the analysis of the primary completion data?	Yes
Primary completion date	25 February 2011
Global end of trial reached?	Yes
Global end of trial date	29 July 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the non-inferiority of MenACWY-TT (Lot A) vaccine when compared to MenACWY-DT vaccine in terms of the percentage of subjects with serum bactericidal assay using human complement against Neisseria meningitides serogroup A (hSBA-MenA), serogroup C (hSBA-MenC), serogroup W-135 (hSBA-MenW-135) and serogroup Y (hSBA-MenY) vaccine response one month after vaccination.

Protection of trial subjects:

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.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 August 2010
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: 713
Country: Number of subjects enrolled	Canada: 300
Worldwide total number of subjects	1013
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)	0
Adolescents (12-17 years)	1013

Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

During the screening the following steps occurred: check for inclusion/exclusion criteria, contraindications/precautions, medical history of the subjects and signing informed consent forms. Out of the 1013 subjects enrolled in this study, 2 were assigned subject numbers but received no vaccination and were hence excluded from the study start.

Pre-assignment period milestones

Number of subjects started	1013
Number of subjects completed	1011

Pre-assignment subject non-completion reasons

Reason: Number of subjects	No vaccination received: 2

Period 1

Period 1 title	Overall (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:

Data were collected in an observer-blind manner during this study. The blinding was observer-blind with respect to lots of MenACWY-TT and observer-blind with respect to MenACWY-TT or Menactra. By observer-blind, it was meant that during the course of the study, the vaccine recipient and those responsible for the evaluation of any study endpoint (e.g. safety and reactogenicity) were all unaware of which vaccine was administered.

Arms

Are arms mutually exclusive?	Yes
Arm title	Nimenrix A Group

Arm description:

Healthy male and female subjects between, and including, 10 and 25 years of age, who received 1 dose of Nimenrix Lot A vaccine, administered intramuscularly in the deltoid region of the non-dominant arm.

Arm type	Experimental
Investigational medicinal product name	Nimenrix
Investigational medicinal product code	
Other name	Meningococcal vaccine GSK 134612
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

One intramuscular injection administered in the deltoid region of the non-dominant arm.

Arm title	Nimenrix B Group

Arm description:

Healthy male and female subjects between, and including, 10 and 25 years of age, who received 1 dose of Nimenrix Lot B vaccine, administered intramuscularly in the deltoid region of the non-dominant arm.

Arm type	Experimental

Investigational medicinal product name	Nimenrix
Investigational medicinal product code	
Other name	Meningococcal vaccine GSK 134612
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

One intramuscular injection administered in the deltoid region of the non-dominant arm.

Arm title	Menactra Group

Arm description:

Healthy male and female subjects between, and including, 10 and 25 years of age, who received 1 dose of Menactra vaccine, administered intramuscularly in the deltoid region of the non-dominant arm.

Arm type	Active comparator
Investigational medicinal product name	Menactra
Investigational medicinal product code	
Other name	MenACWY-DT vaccine
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

One intramuscular injection administered in the deltoid region of the non-dominant arm.

Number of subjects in period 1[1]	Nimenrix A Group	Nimenrix B Group	Menactra Group
Started	337	336	338
Completed	327	326	324
Not completed	10	10	14
Subjects unreachable	1	-	-
Consent withdrawn by subject	-	2	2
Subject incarcerated	-	1	-
Extended holiday	-	-	1
Lost to follow-up	9	7	10
Subject refuses visit 2	-	-	1

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Out of the 1013 subjects enrolled in this study, 2 were assigned subject numbers but received no vaccination and were hence excluded from the study start.

Baseline characteristics

Reporting groups	
Reporting group title	Nimenrix A Group
Reporting group description:	
Healthy male and female subjects between, and including, 10 and 25 years of age, who received 1 dose of Nimenrix Lot A vaccine, administered intramuscularly in the deltoid region of the non-dominant arm.	
Reporting group title	Nimenrix B Group
Reporting group description:	
Healthy male and female subjects between, and including, 10 and 25 years of age, who received 1 dose of Nimenrix Lot B vaccine, administered intramuscularly in the deltoid region of the non-dominant arm.	
Reporting group title	Menactra Group
Reporting group description:	
Healthy male and female subjects between, and including, 10 and 25 years of age, who received 1 dose of Menactra vaccine, administered intramuscularly in the deltoid region of the non-dominant arm.	

Reporting group values	Nimenrix A Group	Nimenrix B Group	Menactra Group
Number of subjects	337	336	338
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous Units: years			
arithmetic mean	16.4	16.3	16.2
standard deviation	± 5.16	± 5.16	± 4.97
Gender categorical Units: Subjects			
Female	175	169	176
Male	162	167	162
Race/Ethnicity Units: Subjects			
African heritage/African American	38	29	40
American Indian or Alaskan native	4	2	1
Asian-Central/South Asian heritage	17	17	17
Asian-East Asian heritage	4	3	5
Asian-Japanese heritage	0	2	0
Asian-South East Asian heritage	4	3	2
White-Arabic/North African heritage	2	3	2
White-Caucasian/European heritage	248	249	257
Other (Mix of races, e.g. African/White)	20	28	14

Reporting group values	Total		
Number of subjects	1011		
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			
standard deviation	-		
Gender categorical Units: Subjects			
Female	520		
Male	491		
Race/Ethnicity Units: Subjects			
African heritage/African American	107		
American Indian or Alaskan native	7		
Asian-Central/South Asian heritage	51		
Asian-East Asian heritage	12		
Asian-Japanese heritage	2		
Asian-South East Asian heritage	9		
White-Arabic/North African heritage	7		
White-Caucasian/European heritage	754		
Other (Mix of races, e.g. African/White)	62		

End points

End points reporting groups

Reporting group title	Nimenrix A Group
Reporting group description:	
Healthy male and female subjects between, and including, 10 and 25 years of age, who received 1 dose of Nimenrix Lot A vaccine, administered intramuscularly in the deltoid region of the non-dominant arm.	

Reporting group title	Nimenrix B Group
Reporting group description:	
Healthy male and female subjects between, and including, 10 and 25 years of age, who received 1 dose of Nimenrix Lot B vaccine, administered intramuscularly in the deltoid region of the non-dominant arm.	

Reporting group title	Menactra Group
Reporting group description:	
Healthy male and female subjects between, and including, 10 and 25 years of age, who received 1 dose of Menactra vaccine, administered intramuscularly in the deltoid region of the non-dominant arm.	

Primary: Number of subjects with vaccine response to serum bactericidal assay using human complement against Neisseria meningitidis serogroup A, C, W-135 and Y (hSBA-MenA, hSBA-MenC, hSBA-MenW-135 and hSBA-MenY) antibodies

End point title	Number of subjects with vaccine response to serum bactericidal assay using human complement against Neisseria meningitidis serogroup A, C, W-135 and Y (hSBA-MenA, hSBA-MenC, hSBA-MenW-135 and hSBA-MenY) antibodies[1][2]
End point description:	
Vaccine response was defined as: -for initially seronegative subjects [with hSBA titer below (<) 1:4]: post-vaccination antibody titer greater than or equal to (≥) 1:8 one month after vaccination; -for initially seropositive subjects (with hSBA titer ≥ 1:4): post-vaccination antibody titer ≥ 4-fold the pre-vaccination antibody titer one month after vaccination.	
End point type	Primary
End point timeframe:	
One month after the vaccination (Month 1)	

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 analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.
[2] - 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: Reporting for hSBA results was done separately for the baseline groups.

End point values	Nimenrix A Group	Menactra Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	310	297		
Units: Subjects				
hSBA-MenA [N=310;297]	218	191		
hSBA-MenC [N=281;274]	217	209		
hSBA-MenW-135 [N=279;289]	198	185		
hSBA-MenY [N=293;295]	150	115		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with hSBA-MenA, hSBA-MenC, hSBA-MenW-135 and hSBA-MenY antibody titers ≥ the cut-off value

End point title	Number of subjects with hSBA-MenA, hSBA-MenC, hSBA-MenW-135 and hSBA-MenY antibody titers ≥ the cut-off value

End point description:

The cut-off value for the hSBA-Men titers was greater than or equal to (≥) 1:4.

End point type	Secondary

End point timeframe:

Prior to (PRE) and one month after vaccination (Month 1)

End point values	Nimenrix A Group	Nimenrix B Group	Menactra Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	315	309	306	
Units: Subjects				
hSBA-MenA, PRE [N=310;309;306]	79	84	89	
hSBA-MenA, Month 1 [N=315;309;305]	253	243	223	
hSBA-MenC, PRE [N=288;286;289]	175	188	197	
hSBA-MenC, Month 1 [N=307;304;296]	295	293	291	
hSBA-MenW-135, PRE [N=293;290;299]	99	98	102	
hSBA-MenW-135, Month 1 [N=298;292;297]	272	262	247	
hSBA-MenY, PRE [N=296;306;304]	215	224	234	
hSBA-MenY, Month 1 [N=313;307;305]	307	302	287	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with hSBA-MenA, hSBA-MenC, hSBA-MenW-135 and hSBA-MenY antibody titers ≥ the cut-off value

End point title	Number of subjects with hSBA-MenA, hSBA-MenC, hSBA-MenW-135 and hSBA-MenY antibody titers ≥ the cut-off value

End point description:

The cut-off value for the hSBA-Men titers was greater than or equal to (≥) 1:8.

End point type	Secondary

End point timeframe:

Prior to (PRE) and one month after vaccination (Month 1)

End point values	Nimenrix A Group	Nimenrix B Group	Menactra Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	315	309	306	
Units: Subjects				
hSBA-MenA, PRE [N=310;309;306]	61	65	67	
hSBA-MenA, Month 1 [N=315;309;305]	251	242	221	
hSBA-MenC, PRE [N=288;286;289]	174	185	193	
hSBA-MenC, Month 1 [N=307;304;296]	295	292	291	
hSBA-MenW-135, PRE [N=293;290;299]	99	97	101	
hSBA-MenW-135, Month 1 [N=298;292;297]	272	262	247	
hSBA-MenY, PRE [N=296;306;304]	215	223	234	
hSBA-MenY, Month 1 [N=313;307;305]	307	302	287	

Statistical analyses

No statistical analyses for this end point

Secondary: hSBA-MenA, hSBA-MenC, hSBA-MenW-135 and hSBA-MenY antibody titers

End point title	hSBA-MenA, hSBA-MenC, hSBA-MenW-135 and hSBA-MenY antibody titers
End point description:	
Antibody titers are presented as geometric mean titers (GMTs).	
End point type	Secondary
End point timeframe:	
Prior to (PRE) and one month after vaccination (Month 1)	

End point values	Nimenrix A Group	Nimenrix B Group	Menactra Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	315	309	306	
Units: Titers				
geometric mean (confidence interval 95%)				
hSBA-MenA, PRE [N=310;309;306]	3.6 (3.1 to 4.0)	3.6 (3.2 to 4.1)	3.6 (3.2 to 4.1)	
hSBA-MenA, Month 1 [N=315;309;305]	54.2 (43.5 to 67.4)	49.6 (39.6 to 62.1)	41.3 (32.3 to 52.9)	
hSBA-MenC, PRE [N=288;286;289]	15.6 (12.3 to 19.9)	16.0 (12.8 to 20.0)	18.0 (14.4 to 22.6)	
hSBA-MenC, Month 1 [N=307;304;296]	687.1 (510.5 to 924.9)	755.8 (557.3 to 1025.0)	543.3 (411.2 to 718.0)	
hSBA-MenW-135, PRE [N=293;290;299]	7.7 (6.1 to 9.7)	7.6 (6.0 to 9.6)	7.4 (5.9 to 9.2)	
hSBA-MenW-135, Month 1 [N=298;292;297]	174.5 (138.6 to 219.6)	161.6 (128.3 to 203.5)	101.7 (77.9 to 132.7)	
hSBA-MenY, PRE [N=296;306;304]	45.7 (35.9 to 58.2)	49.8 (39.1 to 63.4)	55.3 (43.7 to 69.9)	

hSBA-MenY, Month 1 [N=313;307;305]	349.1 (298.1 to 408.8)	387.4 (329.7 to 455.1)	253.8 (204.9 to 314.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with vaccine response for hSBA antibodies

End point title	Number of subjects with vaccine response for hSBA

End point description:

End point type	Secondary

End point timeframe:

One month after vaccination

Notes:

[3] - 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: Reporting for hSBA results was done separately for the baseline groups.

End point values	Nimenrix B Group			
Subject group type	Reporting group			
Number of subjects analysed	300			
Units: Subjects				
hSBA-MenA [N=300]	214			
hSBA-MenC [N=274]	226			
hSBA-MenW-135 [N=270]	196			
hSBA-MenY [N=294]	150			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any and grade 3 solicited local symptoms

End point title	Number of subjects with any and grade 3 solicited local symptoms

End point description:

Assessed solicited local symptoms were pain, redness and swelling. Any = occurrence of the symptom regardless of intensity grade. Grade 3 pain = pain that prevented normal activity. Grade 3 redness/swelling = redness/swelling spreading beyond 50 millimeters (mm) of injection site. Relationship analysis was not performed.

End point type	Secondary

End point timeframe:

Within 4 days (Day 0 - Day 3) following vaccination

End point values	Nimenrix A Group	Nimenrix B Group	Menactra Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	329	329	325	
Units: Subjects				
Any Pain [N=329;329;325]	169	167	180	
Grade 3 Pain [N=329;329;325]	8	5	2	
Any Redness [N=329;329;325]	85	60	66	
Grade 3 Redness [N=329;329;325]	3	2	6	
Any Swelling [N=329;329;325]	63	40	44	
Grade 3 Swelling [N=329;329;325]	3	3	3	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any, grade 3 and related solicited general symptoms

End point title	Number of subjects with any, grade 3 and related solicited general symptoms

End point description:

Assessed solicited general symptoms were fatigue, gastrointestinal, headache and temperature [defined as oral temperature equal to or above 37.5 degrees Celsius (°C)]. Any = occurrence of the symptom regardless of intensity grade. Grade 3 symptom = symptom that prevented normal activity. Grade 3 fever = fever > 39.5 °C. Related = symptom assessed by the investigator as related to the vaccination.

End point type	Secondary

End point timeframe:

Within 4 days (Day 0 - Day 3) following vaccination

End point values	Nimenrix A Group	Nimenrix B Group	Menactra Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	329	329	326	
Units: Subjects				
Any Fatigue [N=329;329;326]	96	94	89	
Grade 3 Fatigue [N=329;329;326]	9	7	5	
Related Fatigue [N=329;329;326]	75	80	77	
Any Gastrointestinal [N=329;329;326]	43	43	44	
Grade 3 Gastrointestinal [N=329;329;326]	4	3	4	
Related Gastrointestinal [N=329;329;326]	31	33	32	
Any Headache [N=329;329;326]	86	87	83	
Grade 3 Headache [N=329;329;326]	5	2	6	
Related Headache [N=329;329;326]	72	70	68	

Any Temperature (orally) [N=329;329;326]	17	14	16	
Grade 3 Temperature (orally) [N=329;329;326]	1	0	0	
Related Temperature (orally) [N=329;329;326]	15	10	12	

Statistical analyses

No statistical analyses for this end point

Secondary: Occurrence of unsolicited non-serious Adverse Events (AEs)

End point title	Occurrence of unsolicited non-serious Adverse Events (AEs)

End point description:

An unsolicited AE covers any untoward medical occurrence in a clinical investigation subject temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product and reported in addition to those solicited during the clinical study and any solicited symptom with onset outside the specified period of follow-up for solicited symptoms. Any was defined as the occurrence of any unsolicited AE regardless of intensity grade or relation to vaccination. Grade 3 AE = an AE which prevented normal, everyday activities. Related = AE assessed by the investigator as related to the vaccination.

End point type	Secondary

End point timeframe:

Within 31 days (Day 0 to 30) following vaccination

End point values	Nimenrix A Group	Nimenrix B Group	Menactra Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	337	336	338	
Units: Subjects				
Any AE(s)	105	76	85	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with occurrence of New Onset of Chronic Illness(es) [NOCI(s)]

End point title	Number of subjects with occurrence of New Onset of Chronic Illness(es) [NOCI(s)]

End point description:

NOCIs include autoimmune disorders, asthma, type I diabetes, allergies.

End point type	Secondary

End point timeframe:

From Month 0 through Month 6

End point values	Nimenrix A Group	Nimenrix B Group	Menactra Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	337	336	338	
Units: Subjects				
Any NOCI(s)	3	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with Serious Adverse Events (SAEs)

End point title	Number of subjects with Serious Adverse Events (SAEs)

End point description:

SAEs assessed include medical occurrences that result in death, are life-threatening, require hospitalization or prolongation of hospitalization or result in disability/incapacity.

End point type	Secondary

End point timeframe:

From Month 0 through Month 6

End point values	Nimenrix A Group	Nimenrix B Group	Menactra Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	337	336	338	
Units: Subjects				
All SAEs	1	5	2	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited local and general symptoms: during the 4-day (Days 0-3) post-vaccination period. Unsolicited AEs: during the 31-day (Days 0-30) post-vaccination period. SAEs: during the entire study period (from Month 0 up to Month 6).

Adverse event reporting additional description:

The number of occurrences reported for solicited symptoms, adverse events, and serious adverse events were not available for posting. The number of subjects affected by each specific event was indicated as the number of occurrences.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	10.0

Reporting groups

Reporting group title	Nimenrix A Group

Reporting group description:

Healthy male and female subjects between, and including, 10 and 25 years of age, who received 1 dose of Nimenrix Lot A vaccine, administered intramuscularly in the deltoid region of the non-dominant arm.

Reporting group title	Nimenrix B Group

Reporting group description:

Healthy male and female subjects between, and including, 10 and 25 years of age, who received 1 dose of Nimenrix Lot B vaccine, administered intramuscularly in the deltoid region of the non-dominant arm.

Reporting group title	Menactra Group

Reporting group description:

Healthy male and female subjects between, and including, 10 and 25 years of age, who received 1 dose of Menactra vaccine, administered intramuscularly in the deltoid region of the non-dominant arm.

Serious adverse events	Nimenrix A Group	Nimenrix B Group	Menactra Group
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 337 (0.30%)	5 / 336 (1.49%)	2 / 338 (0.59%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Jaw fracture			
subjects affected / exposed	0 / 337 (0.00%)	0 / 336 (0.00%)	1 / 338 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haematoma			
subjects affected / exposed	0 / 337 (0.00%)	0 / 336 (0.00%)	1 / 338 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 337 (0.30%)	1 / 336 (0.30%)	0 / 338 (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
Hypoxia			
subjects affected / exposed	0 / 337 (0.00%)	1 / 336 (0.30%)	0 / 338 (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			
Appendicitis			
subjects affected / exposed	0 / 337 (0.00%)	2 / 336 (0.60%)	0 / 338 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 337 (0.00%)	2 / 336 (0.60%)	0 / 338 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	0 / 337 (0.00%)	1 / 336 (0.30%)	0 / 338 (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
Tooth infection			
subjects affected / exposed	0 / 337 (0.00%)	1 / 336 (0.30%)	0 / 338 (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

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

Non-serious adverse events	Nimenrix A Group	Nimenrix B Group	Menactra Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	232 / 337 (68.84%)	219 / 336 (65.18%)	234 / 338 (69.23%)
General disorders and administration site conditions			

Pain			
alternative assessment type: Systematic			
subjects affected / exposed[1]	169 / 329 (51.37%)	167 / 329 (50.76%)	180 / 325 (55.38%)
occurrences (all)	169	167	180
Redness			
alternative assessment type: Systematic			
subjects affected / exposed[2]	85 / 329 (25.84%)	60 / 329 (18.24%)	66 / 325 (20.31%)
occurrences (all)	85	60	66
Swelling			
alternative assessment type: Systematic			
subjects affected / exposed[3]	63 / 329 (19.15%)	40 / 329 (12.16%)	44 / 325 (13.54%)
occurrences (all)	63	40	44
Fatigue			
alternative assessment type: Systematic			
subjects affected / exposed[4]	96 / 329 (29.18%)	94 / 329 (28.57%)	89 / 326 (27.30%)
occurrences (all)	96	94	89
Gastrointestinal			
alternative assessment type: Systematic			
subjects affected / exposed[5]	43 / 329 (13.07%)	43 / 329 (13.07%)	44 / 326 (13.50%)
occurrences (all)	43	43	44
Headache			
alternative assessment type: Systematic			
subjects affected / exposed[6]	86 / 329 (26.14%)	87 / 329 (26.44%)	83 / 326 (25.46%)
occurrences (all)	86	87	83
Temperature (Orally)			
alternative assessment type: Systematic			
subjects affected / exposed[7]	17 / 329 (5.17%)	14 / 329 (4.26%)	16 / 326 (4.91%)
occurrences (all)	17	14	16

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.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 March 2010	Amendment 3 The introduction was updated with the current licensing status of competitor vaccines and the current recommendations for meningococcal vaccines. The primary objective of the current study is to demonstrate the non-inferiority of MenACWY-TT (Lot A) when compared to Menactra at 10-25 years of age in terms of the percentage of subjects with hSBA-MenA, hSBA-MenC, hSBA-MenW-135, and hSBA-MenY vaccine response* one month after vaccination. *Vaccine response is defined as an hSBA titer of at least 1:8 in subjects initially seronegative (hSBA titer <1:4) and as a 4-fold increase in titer in subjects initially seropositive (hSBA titer 1:4). In addition, to support the data obtained by hSBA testing, antibody concentrations against meningococcal polysaccharides were planned to be assessed by ELISA. The sponsor decided not to perform the ELISA testing for the following reasons: • the World Health Organisation (WHO) considers SBA the primary means of assessing immune response to meningoccoccal conjugate vaccines [WHO, 2006;WHO, 1999] • circulating bactericidal antibodies are more critical for persistent protection against meningococcal disease than non-functional antibodies against meningococcal polysaccharides [CDC, 2011; WHO, 2006]. Section 6.2 (Storage and handling of study vaccines) has been modified in order to align the wording with the new version of SOP-BIO-CLIN-7055 v04 entitled "Management of the Cold Chain for GlaxoSmithKline Biologicals investigational human subject research" effective since 31 March 2010.
06 September 2010	• The MenA capsular polysaccharide O-acetylation in MenACWY-TT vaccine Lot A will be 68% instead of 61%. • Mencevax™ ACWY is not licensed in Canada. • Menveo® (Novartis' meningococcal [groups A, C, Y and W-135] oligosaccharide diphtheria CRM197 conjugate vaccine) was recently licensed in Canada. • A new abbreviation was added to the List of Abbreviations. • For clarification, the word "days" was added after "180-210" in Table 3 Intervals between study visits. • For clarification, the 31-day post-vaccination reporting period for pregnancies was added to Figure 1. • New safety reporting telephone numbers replaced the old numbers. New study contact for emergency code break telephone numbers replaced the old numbers.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported