Clinical trial results:
A phase II, open, controlled, multi-center study to evaluate the long-term antibody persistence at 1 year, 3 years and 5 years after the administration of one dose of GlaxoSmithKline (GSK) Biologicals' meningococcal serogroups A, C, W-135, Y-tetanus toxoid conjugate (MenACWY-TT) vaccine versus one dose of sanofi-pasteur's meningococcal serogroups A, C, W-135 and Y-diphtheria toxoid conjugate vaccine (Menactra®) in healthy adolescents/adults aged 10-25 years and to evaluate the safety and immunogenicity of a booster response to MenACWY-TT vaccine administered at 5 years post-primary vaccination with MenACWY-TT or Menactra® and of a primary vaccination of MenACWY-TT in a newly enrolled group aged 15-<31 years.

Summary

EudraCT number	2012-002718-38
Trial protocol	Outside EU/EEA
Global end of trial date	20 September 2013

Results information

Result version number	v1 (current)
This version publication date	11 May 2016
First version publication date	18 July 2015

Trial information

Trial identification

Sponsor protocol code	111670

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00715910
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, 044 2089-904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089-904466, 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	15 April 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 April 2013
Global end of trial reached?	Yes
Global end of trial date	20 September 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the long-term persistence of the immunogen-icity induced by MenACWY-TT vaccine as compared to Menactra at 11-25 years of age in terms of the percentage of subjects with N. meningitidis serogroup A (MenA), N. meningitidis serogroup C (MenC), N. meningitidis serogroup W-135 (MenW-135), and N. meningitidis serogroup Y (MenY) titers >= 1:8 as measured by a serum bactericidal assay using human complement (hSBA).

Protection of trial subjects:

The vaccines were observed closely for at least 30 minutes following the administration of the vaccines, with appropriate medical treatment readily available in case of a rare anaphylactoid/anaphylactic reaction.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 July 2008
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy, Safety
Long term follow-up duration	5 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 648
Worldwide total number of subjects	648
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	68
Adults (18-64 years)	580
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.

Period 1

Period 1 title	Persistence Phase Year 1
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Nimenrix 1 Group

Arm description:

Subjects 11-25 years of age who were previously vaccinated with 1 dose of Nimenrix vaccine at the time of vaccination.

Arm type	Experimental
Investigational medicinal product name	Nimenrix™
Investigational medicinal product code	
Other name	Meningococcal vaccine GSK134612 (MenACWY-TT)
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

One dose, as intramuscular injection.

Arm title	Menactra Group

Arm description:

Subjects 11-25 years of age who were previously vaccinated with 1 dose of Menactra® vaccine at the time of vaccination.

Arm type	Active comparator
Investigational medicinal product name	Menactra®
Investigational medicinal product code	MenACWY-DT
Other name	Sanofi Pasteur’s meningococcal serogroups A, C, W-135 and Y diphtheria toxoid conjugate vaccine.
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

One dose, as intramuscular injection.

Arm title	Nimenrix 2 Group

Arm description:

Subjects 10<11 years of age who were previously vaccinated with 1 dose of Nimenrix vaccine at the time of vaccination.

Arm type	Experimental

Investigational medicinal product name	Nimenrix™
Investigational medicinal product code	
Other name	Meningococcal vaccine GSK134612 (MenACWY-TT)
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

One dose, as intramuscular injection.

Number of subjects in period 1	Nimenrix 1 Group	Menactra Group	Nimenrix 2 Group
Started	433	147	68
Completed	433	147	68

Period 2

Period 2 title	Persistence Phase Year 3
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Nimenrix 1 Group

Arm description:

Subjects 11-25 years of age who were previously vaccinated with 1 dose of Nimenrix vaccine at the time of vaccination.

Arm type	Experimental
Investigational medicinal product name	Nimenrix™
Investigational medicinal product code	
Other name	Meningococcal vaccine GSK134612 (MenACWY-TT)
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

One dose, as intramuscular injection.

Arm title	Menactra Group

Arm description:

Subjects 11-25 years of age who were previously vaccinated with 1 dose of Menactra® vaccine at the time of vaccination.

Arm type	Active comparator
Investigational medicinal product name	Menactra®
Investigational medicinal product code	MenACWY-DT
Other name	Sanofi Pasteur's meningococcal serogroups A, C, W-135 and Y diphtheria toxoid conjugate vaccine.
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

One dose, as intramuscular injection.

Arm title	Nimenrix 2 Group

Arm description:

Subjects 10<11 years of age who were previously vaccinated with 1 dose of Nimenrix vaccine at the time of vaccination.

Arm type	Experimental
Investigational medicinal product name	Nimenrix™
Investigational medicinal product code	
Other name	Meningococcal vaccine GSK134612 (MenACWY-TT)
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

One dose, as intramuscular injection.

Number of subjects in period 2[1]	Nimenrix 1 Group	Menactra Group	Nimenrix 2 Group
Started	345	86	56
Completed	345	86	56

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Not all study participants returned in time for every study visit, but they were allowed to continue the study nonetheless. The number of participants who started each study period depends on the actual rate of return of the subjects.

Period 3

Period 3 title	Persistence Phase Year 5
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Nimenrix 1 Group

Arm description:

Subjects 11-25 years of age who were previously vaccinated with 1 dose of Nimenrix vaccine at the time of vaccination.

Arm type	Experimental
Investigational medicinal product name	Nimenrix™
Investigational medicinal product code	
Other name	Meningococcal vaccine GSK134612 (MenACWY-TT)
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Intramuscular use

Arms

Arm title	Menactra Booster Group

Arm description:

Subjects 11-25 years of age who had received 1 dose of Menactra vaccine in primary study (NCT00454909) and will receive 1 dose of Nimenrix vaccine in this current study.

Arm type	Active comparator
Investigational medicinal product name	Nimenrix™
Investigational medicinal product code	
Other name	Meningococcal vaccine GSK134612 (MenACWY-TT)
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

One dose, as intramuscular injection.

Number of subjects in period 4[3]	Menactra Booster Group
Started	38
Completed	37
Not completed	1
Lost to follow-up	1

Notes:

[3] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Not all study participants returned in time for every study visit, but they were allowed to continue the study nonetheless. The number of participants who started each study period depends on the actual rate of return of the subjects.

Baseline characteristics

Reporting groups	
Reporting group title	Nimenrix 1 Group
Reporting group description:	
Subjects 11-25 years of age who were previously vaccinated with 1 dose of Nimenrix vaccine at the time of vaccination.	
Reporting group title	Menactra Group
Reporting group description:	
Subjects 11-25 years of age who were previously vaccinated with 1 dose of Menactra® vaccine at the time of vaccination.	
Reporting group title	Nimenrix 2 Group
Reporting group description:	
Subjects 10<11 years of age who were previously vaccinated with 1 dose of Nimenrix vaccine at the time of vaccination.	

Reporting group values	Nimenrix 1 Group	Menactra Group	Nimenrix 2 Group
Number of subjects	433	147	68
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	15.9	16	11.2
standard deviation	± 2.79	± 2.83	± 0.42
Gender categorical			
Units: Subjects			
Female	213	78	41
Male	220	69	27

Reporting group values	Total		
Number of subjects	648		
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	332		
Male	316		

End points

End points reporting groups

Reporting group title	Nimenrix 1 Group

Reporting group description:

Subjects 11-25 years of age who were previously vaccinated with 1 dose of Nimenrix vaccine at the time of vaccination.

Reporting group title	Menactra Group

Reporting group description:

Subjects 11-25 years of age who were previously vaccinated with 1 dose of Menactra® vaccine at the time of vaccination.

Reporting group title	Nimenrix 2 Group

Reporting group description:

Subjects 10<11 years of age who were previously vaccinated with 1 dose of Nimenrix vaccine at the time of vaccination.

Reporting group title	Nimenrix 1 Group

Reporting group description:

Subjects 11-25 years of age who were previously vaccinated with 1 dose of Nimenrix vaccine at the time of vaccination.

Reporting group title	Menactra Group

Reporting group description:

Subjects 11-25 years of age who were previously vaccinated with 1 dose of Menactra® vaccine at the time of vaccination.

Reporting group title	Nimenrix 2 Group

Reporting group description:

Subjects 10<11 years of age who were previously vaccinated with 1 dose of Nimenrix vaccine at the time of vaccination.

Reporting group title	Nimenrix 1 Group

Reporting group description:

Subjects 11-25 years of age who were previously vaccinated with 1 dose of Nimenrix vaccine at the time of vaccination.

Reporting group title	Menactra Group

Reporting group description:

Subjects 11-25 years of age who were previously vaccinated with 1 dose of Menactra® vaccine at the time of vaccination.

Reporting group title	Nimenrix 2 Group

Reporting group description:

Subjects 10<11 years of age who were previously vaccinated with 1 dose of Nimenrix vaccine at the time of vaccination.

Reporting group title	Menactra Booster Group

Reporting group description:

Subjects 11-25 years of age who had received 1 dose of Menactra vaccine in primary study (NCT00454909) and will receive 1 dose of Nimenrix vaccine in this current study.

Subject analysis set title	Nimenrix Pooled Group
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Pooled group of subjects 10-25 years of age from Nimenrix 1 and Nimenrix 2 groups in the primary study (NCT00454909) who had received 1 dose of Nimenrix vaccine in that study and will receive a booster dose in this current study.

Subject analysis set title	Nimenrix Naïve Group
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Subjects 15 to <31 years of age at the time of primary vaccination with 1 dose of Nimenrix vaccine at year 5 of the current study.

Primary: Number of subjects with serum bactericidal assay (using human complement) (hSBA) titers equal to or above the cut-off values.

End point title	Number of subjects with serum bactericidal assay (using human complement) (hSBA) titers equal to or above the cut-off values.[1]

End point description:

hSBA antibody titers were assessed for the hSBA-MenA, hSBA-MenC, hSBA-MenW-135, and hSBA-MenY serogroups respectively. The antibody cut-off value assessed was equal to or above 1:8.

End point type	Primary

End point timeframe:

At year 1 persistence.

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.

End point values	Nimenrix 1 Group	Menactra Group	Nimenrix 2 Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	356	112	58	
Units: Subjects				
hSBA-MenA [N=350;111;57]	102	35	15	
hSBA-MenC [N=336;105;56]	319	77	55	
hSBA-MenW-135 [N=327;107;54]	322	81	53	
hSBA-MenY [N=356;112;58]	348	97	58	

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with hSBA titers equal to or above the cut-off values.

End point title	Number of subjects with hSBA titers equal to or above the cut-off values.[2]

End point description:

hSBA antibody titers were assessed for the hSBA-MenA, hSBA-MenC, hSBA-MenW-135, and hSBA-MenY serogroups respectively. The antibody cut-off value assessed was equal to or above 1:8.

End point type	Primary

End point timeframe:

At year 3 persistence.

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 analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	Nimenrix 1 Group	Menactra Group	Nimenrix 2 Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	321	80	53	
Units: Subjects				
hSBA-MenA [N=314;78;51]	117	37	22	
hSBA-MenC [N=317;80;53]	295	65	51	

hSBA-MenW-135 [N=321;79;53]	306	67	51	
hSBA-MenY [N=319;79;51]	306	70	49	

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with hSBA titers equal to or above the cut-off values.

End point title	Number of subjects with hSBA titers equal to or above the cut-off values.[3]

End point description:

hSBA antibody titers were assessed for the hSBA-MenA, hSBA-MenC, hSBA-MenW-135, and hSBA-MenY serogroups respectively. The antibody cut-off value assessed was equal to or above 1:8.

End point type	Primary

End point timeframe:

At year 5 persistence.

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 analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	Nimenrix 1 Group	Menactra Group	Nimenrix 2 Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	142	45	26	
Units: Subjects				
hSBA-MenA [N=141;45;24]	69	20	9	
hSBA-MenC [N=140;44;26]	130	35	22	
hSBA-MenW-135 [N=138;44;26]	120	37	24	
hSBA-MenY [N=142;44;26]	134	40	24	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with hSBA titers equal to or above the cut-off values.

End point title	Number of subjects with hSBA titers equal to or above the cut-off values.

End point description:

hSBA antibody titers were assessed for the hSBA-MenA, hSBA-MenC, hSBA-MenW-135, and hSBA-MenY serogroups respectively. The antibody cut-off value assessed was equal to or above 1:4.

End point type	Secondary

End point timeframe:

At year 1 persistence

End point values	Nimenrix 1 Group	Menactra Group	Nimenrix 2 Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	356	112	58	
Units: Subjects				
hSBA-MenA [N=350;111;57]	106	35	17	
hSBA-MenC [N=336;105;56]	319	77	55	
hSBA-MenW-135 [N=327;107;54]	322	81	54	
hSBA-MenY [N=356;112;58]	348	97	58	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with hSBA titers equal to or above the cut-off values.

End point title	Number of subjects with hSBA titers equal to or above the cut-off values.

End point description:

hSBA antibody titers were assessed for the hSBA-MenA, hSBA-MenC, hSBA-MenW-135, and hSBA-MenY serogroups respectively. The antibody cut-off value assessed was equal to or above 1:4.

End point type	Secondary

End point timeframe:

At year 3 persistence.

End point values	Nimenrix 1 Group	Menactra Group	Nimenrix 2 Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	321	80	53	
Units: Subjects				
hSBA-MenA [N=314;78;51]	123	37	23	
hSBA-MenC [N=317;80;53]	295	68	51	
hSBA-MenW-135 [N=321;79;53]	307	67	52	
hSBA-MenY [N=319;79;51]	306	70	49	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with hSBA titers equal to or above the cut-off values.

End point title	Number of subjects with hSBA titers equal to or above the cut-

	off values.

End point description:

hSBA antibody titers were assessed for the hSBA-MenA, hSBA-MenC, hSBA-MenW-135, and hSBA-MenY serogroups respectively. The antibody cut-off value assessed was equal to or above 1:4.

End point type	Secondary

End point timeframe:

At year 5 persistence.

End point values	Nimenrix 1 Group	Menactra Group	Nimenrix 2 Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	142	45	26	
Units: Subjects				
hSBA-MenA [N=141;45;24]	74	20	9	
hSBA-MenC [N=140;44;26]	134	39	24	
hSBA-MenW-135 [N=138;44;26]	122	37	24	
hSBA-MenY [N=142;44;26]	134	40	24	

Statistical analyses

No statistical analyses for this end point

Secondary: hSBA antibody titers.

End point title	hSBA antibody titers.

End point description:

Titers are given as geometric mean titers (GMTs) for the serogroups hSBA-MenA, hSBA-MenC, hSBA-MenW-135, and hSBA-MenY respectively.

End point type	Secondary

End point timeframe:

At year 1 persistence.

End point values	Nimenrix 1 Group	Menactra Group	Nimenrix 2 Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	356	112	58	
Units: Titers				
geometric mean (confidence interval 95%)				
hSBA-MenA titers [N=350;111;57]	5.4 (4.5 to 6.4)	6 (4.3 to 8.5)	5.2 (3.4 to 7.9)	
hSBA-MenC titers [N=336;105;56]	172 (142.5 to 207.4)	46.7 (30.2 to 72.1)	238.3 (154 to 368.9)	
hSBA-MenW-135 titers [N=327;107;54]	197.5 (173 to 225.5)	48.9 (32.5 to 73.8)	231.2 (174.5 to 306.2)	
hSBA-MenY titers [N=356;112;58]	271.8 (237.5 to 311.2)	100.8 (69.6 to 146.2)	266.8 (205.1 to 347)	

Statistical analyses

No statistical analyses for this end point

Secondary: hSBA antibody titers.

End point title	hSBA antibody titers.

End point description:

Titers are given as geometric mean titers (GMTs) for the serogroups hSBA-MenA, hSBA-MenC, hSBA-MenW-135, and hSBA-MenY respectively.

End point type	Secondary

End point timeframe:

At year 3 persistence.

End point values	Nimenrix 1 Group	Menactra Group	Nimenrix 2 Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	321	80	53	
Units: Titers				
geometric mean (confidence interval 95%)				
hSBA-MenA titers [N=314;78;51]	6.2 (5.2 to 7.3)	9.3 (6.2 to 14)	8.8 (5.3 to 14.9)	
hSBA-MenC titers [N=317;80;53]	117.9 (94.3 to 147.4)	54.8 (33.9 to 88.9)	131.2 (79.8 to 215.7)	
hSBA-MenW-135 titers [N=321;79;53]	141.6 (122.8 to 163.4)	75.5 (48.7 to 117)	137.6 (98.2 to 192.9)	
hSBA-MenY titers [N=319;79;51]	206.6 (177.9 to 239.8)	139 (93.8 to 206.2)	186.6 (130.7 to 266.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: hSBA antibody titers.

End point title	hSBA antibody titers.

End point description:

Titers are given as geometric mean titers (GMTs) for the serogroups hSBA-MenA, hSBA-MenC, hSBA-MenW-135, and hSBA-MenY respectively.

End point type	Secondary

End point timeframe:

At year 5 persistence.

End point values	Nimenrix 1 Group	Menactra Group	Nimenrix 2 Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	142	45	26	
Units: Titers				
geometric mean (confidence interval 95%)				
hSBA-MenA titers [N=141;45;24]	8.9 (6.8 to 11.8)	7.9 (4.8 to 13.2)	6.3 (3.2 to 12.2)	
hSBA-MenC titers [N=140;44;26]	94.6 (65.9 to 135.9)	30.6 (17.3 to 54.4)	92.9 (39.6 to 217.6)	
hSBA-MenW-135 titers [N=138;44;26]	103.5 (76.3 to 140.5)	70.4 (37.2 to 133.1)	92.4 (50.5 to 168.8)	
hSBA-MenY titers [N=142;44;26]	224.6 (173.9 to 290)	129.3 (77.4 to 215.9)	113.7 (58.4 to 221.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-polysaccharide A (Anti-PSA), anti-PSC, anti-PSY, and anti-PSW-135 concentrations equal to or above the cut-off values.

End point title	Number of subjects with anti-polysaccharide A (Anti-PSA), anti-PSC, anti-PSY, and anti-PSW-135 concentrations equal to or above the cut-off values.

End point description:

The cut-off values were defined as a concentration ≥0.3 microgram per milliliter (µg/mL) and ≥ 2.0 µg/mL.

End point type	Secondary

End point timeframe:

At year 1 persistence.

End point values	Nimenrix 1 Group	Menactra Group	Nimenrix 2 Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	366	112	59	
Units: Subjects				
Anti-PSA ≥ 0.3 µg/mL [N=355;112;56]	340	101	55	
Anti-PSA ≥ 2.0 µg/mL [N=355;112;56]	260	66	38	
Anti-PSC ≥ 0.3 µg/mL [N=366;112;58]	302	56	51	
Anti-PSC ≥ 2.0 µg/mL [N=366;112;58]	162	31	28	
Anti-PSW-135 ≥ 0.3 µg/mL [N=354;104;56]	319	65	54	
Anti-PSW-135 ≥ 2.0 µg/mL [N=354;104;56]	178	27	28	
Anti-PSY ≥ 0.3 µg/mL [N=358;112;59]	342	78	55	
Anti-PSY ≥ 2.0 µg/mL [N=358;112;59]	240	38	37	

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-polysaccharide A (Anti-PSA), anti-PSC, anti-PSY, and anti-PSW-135 antibody concentrations.

End point title	Anti-polysaccharide A (Anti-PSA), anti-PSC, anti-PSY, and anti-PSW-135 antibody concentrations.

End point description:

Antibody concentrations were given as geometric mean concentrations (GMCs) and expressed in µg/mL.

End point type	Secondary

End point timeframe:

At year 1 persistence.

End point values	Nimenrix 1 Group	Menactra Group	Nimenrix 2 Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	366	112	59	
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-PSA [N=355;112;56]	5 (4.2 to 5.9)	3.7 (2.6 to 5.3)	4.2 (2.9 to 6.1)	
Anti-PSC [N=366;112;58]	1.8 (1.5 to 2.1)	0.6 (0.5 to 0.9)	2.1 (1.4 to 3.1)	
Anti-PSW-135 [N=354;104;56]	2 (1.7 to 2.3)	0.8 (0.6 to 1.1)	2 (1.5 to 2.6)	
Anti-PSY [N=358;112;59]	3.4 (3 to 4)	1 (0.7 to 1.3)	2.5 (1.8 to 3.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with serious adverse events (SAEs) related to a concurrent GSK medication.

End point title	Number of subjects with serious adverse events (SAEs) related to a concurrent GSK medication.

End point description:

SAEs assessed include medical occurrences that result in death, are life threatening, require hospitalization or prolongation of hospitalization, result in disability/incapacity or are a congenital anomaly/birth defect in the offspring of a study subject.

End point type	Secondary

End point timeframe:

From 6 months up to 1 year following primary vaccination.

End point values	Nimenrix 1 Group	Menactra Group	Nimenrix 2 Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	433	147	68	
Units: Subjects				
Any SAE(s)	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with SAEs relate

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End point timeframe:

From 6 months up to 5 years following primary vaccination.

End point values	Nimenrix 1 Group	Menactra Group	Nimenrix 2 Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	218	56	38	
Units: Subjects				
Any SAE(s)	0	0	0	

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 equal to or above the cut-off values.

End point title	Number of subjects with hSBA-MenA, hSBA-MenC, hSBA-MenW-135 and hSBA-MenY antibody titers equal to or above the cut-off values.

End point description:

The cut-off values were defined as hSBA antibody titers ≥ 1:4 and ≥ 1:8.

End point type	Secondary

End point timeframe:

1 month post primary (naïve control group) and booster vaccination.

End point values	Menactra Booster Group	Nimenrix Pooled Group	Nimenrix Naïve Group	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	29	109	84	
Units: Subjects				
hSBA-MenA ≥ 1:4 [N=28;106;79]	28	105	61	
hSBA-MenA ≥ 1:8 [N=28;106;79]	28	105	61	
hSBA-MenC ≥ 1:4 [N=29;109;81]	29	108	78	
hSBA-MenC ≥ 1:8 [N=29;109;81]	29	108	77	
hSBA-MenW-135 ≥ 1:4 [N=29;109;80]	29	109	74	
hSBA-MenW-135 ≥ 1:8 [N=29;109;80]	29	109	74	
hSBA-MenY ≥ 1:4 [N=29;109;84]	29	109	82	
hSBA-MenY ≥ 1:8 [N=29;109;84]	29	109	82	

Statistical analyses

No statistical analyses for this end point

Secondary: hSBA antibody titers.

End point title	hSBA antibody titers.

End point description:

Titers are given as GMTs for the serogroups hSBA-MenA, hSBA-MenC, hSBA-MenW-135, and hSBA-MenY respectively.

End point type	Secondary

End point timeframe:

1 month post primary (naïve control group) and booster vaccination.

End point values	Menactra Booster Group	Nimenrix Pooled Group	Nimenrix Naïve Group	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	29	109	84	
Units: Titers				
geometric mean (confidence interval 95%)				
hSBA-MenA [N=28;106;79]	952 (600.9 to 1508.2)	783.8 (601.7 to 1020.9)	79.7 (46.3 to 137.4)	
hSBA-MenC [N=29;109;81]	6722.1 (3950.9 to 11437.2)	5020.4 (3995.4 to 6308.4)	534.7 (308 to 928.1)	
hSBA-MenW-135 [N=29;109;80]	3729 (2415.4 to 5757.1)	5517.6 (4573.6 to 6656.4)	237.7 (150.4 to 375.8)	
hSBA-MenY [N=29;109;84]	6546.4 (4312.3 to 9938)	5664.3 (4590 to 6990.1)	755.1 (522.4 to 1091.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with vaccine response for hSBA-MenA, hSBA-MenC, hSBA-MenW-135 and hSBA-MenY antibodies.

End point title	Number of subjects with vaccine response for hSBA-MenA, hSBA-MenC, hSBA-MenW-135 and hSBA-MenY antibodies.

End point description:

Vaccine response was defined as: For initially seronegative subjects: antibody titre ≥ 1:8 at one month after vaccination For initially seropositive subjects: antibody titre at one month after vaccination ≥ 4 fold the titres before vaccination.

End point type	Secondary

End point timeframe:

1 month post primary (naïve control group) and booster vaccination.

End point values	Menactra Booster Group	Nimenrix Pooled Group	Nimenrix Naïve Group	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	29	106	78	
Units: Subjects				
hSBA-MenA [N=28;101;75]	24	98	51	
hSBA-MenC [N=28;106;68]	27	97	47	
hSBA-MenW-135 [N=28;105;76]	24	101	51	
hSBA-MenY [N=29;106;78]	27	97	53	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with solicited local symptoms.

End point title	Number of subjects with solicited local symptoms.

End point description:

Solicited local symptoms assessed were pain, redness and swelling. Any was defined as occurrence of any solicited local symptom reported irrespective of intensity grade. Grade 3 pain was defined as pain that prevented normal activity. Grade 3 redness and swelling were defined as redness/swelling above 50 millimeter (mm).

End point type	Secondary

End point timeframe:

During the 4-day (Days 0-3) post primary (naïve control group) and booster vaccination.

End point values	Menactra Booster Group			
Subject group type	Reporting group			
Number of subjects analysed	37			
Units: Subjects				
Any Pain	20			
Grade 3 Pain	0			
Any Redness	6			
Grade 3 Redness	0			
Any Swelling	5			
Grade 3 Swelling	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with solicited general symptoms.

End point title	Number of subjects with solicited general symptoms.

End point description:

Solicited general symptoms assessed were fatigue, gastrointestinal symptoms (nausea, vomiting, diarrhea and/or abdominal pain), headache and temperature. Any = occurrence of any general

symptoms reported irrespective of intensity grade and relationship to study vaccination. Any temperature = axillary temperature greater than or equal to (≥)37.5 degrees Celsius (°C). Grade 3 symptoms = symptoms that prevented normal activity. Grade 3 temperature = axillary temperature above 39.0°C. Related = symptoms considered by the investigator to have a causal relationship to vaccination.

End point type	Secondary

End point timeframe:

During the 4-day (Days 0-3) post primary (naïve control group) and booster vaccination.

End point values	Menactra Booster Group			
Subject group type	Reporting group			
Number of subjects analysed	37			
Units: Subjects				
Any Fatigue	7			
Grade 3 Fatigue	0			
Related Fatigue	6			
Any Gastrointestinal symptoms	8			
Grade 3 Gastrointestinal symptoms	0			
Related Gastrointestinal symptoms	8			
Any Headache	10			
Grade 3 Headache	0			
Related Headache	10			
Any Temperature	0			
Grade 3 Temperature	0			
Related Temperature	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with unsolicited adverse events (AEs).

End point title	Number of subjects with unsolicited adverse events (AEs).

End point description:

Unsolicited AE covers any AE 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.

End point type	Secondary

End point timeframe:

During the 31-day (Days 0-30) following primary (naïve control group) and booster vaccination.

End point values	Menactra Booster Group			
Subject group type	Reporting group			
Number of subjects analysed	38			
Units: Subjects				
Any AE(s)	9			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting new onset chronic illness(es) (NOCIs).

End point title	Number of subjects reporting new onset chronic illness(es) (NOCIs).

End point description:

Examples of NOCIs include autoimmune disorders, asthma, type 1 diabetes and allergies.

End point type	Secondary

End point timeframe:

During the 6-month period following the primary (naïve control group) and booster vaccination.

End point values	Menactra Booster Group			
Subject group type	Reporting group			
Number of subjects analysed	38			
Units: Subjects				
Any NOCI(s)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with SAEs.

End point title	Number of subjects with SAEs.

End point description:

SAEs assessed include medical occurrences that result in death, are life threatening, require hospitalization or prolongation of hospitalization, result in disability/incapacity or are a congenital anomaly/birth defect in the offspring of a study subject.

End point type	Secondary

End point timeframe:

During the 6-month period following the primary (naïve control group) and booster vaccination.

End point values	Menactra Booster Group			
Subject group type	Reporting group			
Number of subjects analysed	38			
Units: Subjects				
Any SAE(s)	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

SAEs = From 6 months up to 5 years after primary vaccination and up to 6 months after vaccination in booster phase. Solicited and unsolicited symptoms during 4 days (Days 0-3) and 31-days (Days 0-30) after vaccination in booster phase respectively.

Adverse event reporting additional description:

For the systematically assessed other (non-serious) adverse events, the number of participants at risk included those from Total Vaccinated cohort who had the symptom sheet completed.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups

Reporting group title	Nimenrix Pooled Group

Reporting group description:

Pooled group of subjects 10-25 years of age from Nimenrix 1 and Nimenrix 2 groups in the primary study (NCT00454909) who had received 1 dose of Nimenrix vaccine in that study and will receive a booster dose in this current study.

Reporting group title	Menactra Booster Group

Reporting group description:

Subjects 11-25 years of age who had received 1 dose of Menactra vaccine in primary study (NCT00454909) and received 1 dose of Nimenrix vaccine administered intramuscularly into the non-dominant deltoid in this current study during booster vaccination phase at Year 5.

Reporting group title	Nimenrix Naïve Group

Reporting group description:

Naïve control group of subjects 15 to <31 years at the time of primary vaccination with 1 dose of Nimenrix vaccine administered intramuscularly into the non-dominant deltoid in this current study during booster vaccination phase at Year 5.

Serious adverse events	Nimenrix Pooled Group	Menactra Booster Group	Nimenrix Naïve Group
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 183 (1.64%)	0 / 38 (0.00%)	0 / 101 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 183 (0.55%)	0 / 38 (0.00%)	0 / 101 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			

subjects affected / exposed	1 / 183 (0.55%)	0 / 38 (0.00%)	0 / 101 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malaria			
subjects affected / exposed	1 / 183 (0.55%)	0 / 38 (0.00%)	0 / 101 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Nimenrix Pooled Group	Menactra Booster Group	Nimenrix Naïve Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	100 / 183 (54.64%)	20 / 38 (52.63%)	55 / 101 (54.46%)
General disorders and administration site conditions			
Pain			
alternative assessment type: Systematic			
subjects affected / exposed[1]	100 / 170 (58.82%)	20 / 37 (54.05%)	55 / 91 (60.44%)
occurrences (all)	100	20	55
Redness			
alternative assessment type: Systematic			
subjects affected / exposed[2]	39 / 170 (22.94%)	6 / 37 (16.22%)	17 / 91 (18.68%)
occurrences (all)	39	6	17
Swelling			
alternative assessment type: Systematic			
subjects affected / exposed[3]	27 / 170 (15.88%)	5 / 37 (13.51%)	14 / 91 (15.38%)
occurrences (all)	27	5	14
Fatigue			
alternative assessment type: Systematic			
subjects affected / exposed[4]	58 / 170 (34.12%)	7 / 37 (18.92%)	30 / 91 (32.97%)
occurrences (all)	58	7	30
Gastrointestinal symptoms			
alternative assessment type: Systematic			
subjects affected / exposed[5]	28 / 170 (16.47%)	8 / 37 (21.62%)	20 / 91 (21.98%)
occurrences (all)	28	8	20

Headache			
alternative assessment type: Systematic			
subjects affected / exposed[6]	61 / 170 (35.88%)	10 / 37 (27.03%)	22 / 91 (24.18%)
occurrences (all)	61	10	22
Temperature/(Axillary)			
alternative assessment type: Systematic			
subjects affected / exposed[7]	4 / 170 (2.35%)	0 / 37 (0.00%)	3 / 91 (3.30%)
occurrences (all)	4	0	3
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	3 / 183 (1.64%)	2 / 38 (5.26%)	0 / 101 (0.00%)
occurrences (all)	3	2	0

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
11 May 2011	The primary objective of the current study is to evaluate the long-term persistence of the immunogenicity induced by MenACWY-TT vaccine as compared to Menactra at 11-25 years of age in terms of the percentage of subjects with N. meningitidis serogroup A, C; W-135 and Y titers 1:8 as measured by a serum bactericidal assay using human complement (hSBA) at 1, 3 and 5 year after vaccine administration. In addition, to support the data obtained by hSBA testing, antibody concentrations against meningococcal polysaccharides are planned to be assessed by ELISA. The ELISA testing will be performed at 1 year after vaccine administration, but the sponsor decided not to perform the ELISA testing at 3 and 5 years after vaccine administration for the following reasons: - the World Health Organization (WHO) considers SBA the primary means of assessing immune response to meningococcal conjugate vaccines. - circulating bactericidal antibodies are more critical for persistent protection against meningococcal disease than non- functional antibodies against meningococcal polysaccharides.
01 December 2011	The instructions on reconstitution of the MenACWY-TT vaccine have been updated.
16 February 2012	The co-ordinating author and several contributing author's names have been changed. The saline diluent to reconstitute the MenACWY-TT vaccine has been changed from vial presentation to a pre-filled syringe.
02 May 2012	The Interval for coming back for the Year 5 post-vaccination visit (Visit 3) has been extended 4 weeks, from 5 years + 16 weeks post-vaccination to 5 years + 20 week post-vaccination. This was done because a booster vaccination will also be administered at this visit, and the extension was needed to ensure that vaccine would be available at the study site.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported