



## 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	v1
This version publication date	11 May 2016
First version publication date	29 July 2015

## 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 meningitidis* 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.

### 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
<b>Arm title</b>	Nimenrix™ A Group

Arm description:

Subjects received 1 dose of Nimenrix™ Lot A vaccine.

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.

<b>Arm title</b>	Nimenrix™ B Group
------------------	-------------------

Arm description:

Subjects received 1 dose of Nimenrix™ Lot B vaccine.

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.	
<b>Arm title</b>	Menactra®MenACWY-DT Group

Arm description:

Subjects were vaccinated with Menactra®

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.

<b>Number of subjects in period 1</b> <sup>[1]</sup>	Nimenrix™ A Group	Nimenrix™ B Group	Menactra®MenACWY-DT Group
Started	337	336	338
Completed	327	326	324
Not completed	10	10	14
Consent withdrawn by subject	-	2	2
'Subjects unreachable '	1	-	-
'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:	
Subjects received 1 dose of Nimenrix™ Lot A vaccine.	
Reporting group title	Nimenrix™ B Group
Reporting group description:	
Subjects received 1 dose of Nimenrix™ Lot B vaccine.	
Reporting group title	Menactra®MenACWY-DT Group
Reporting group description:	
Subjects were vaccinated with Menactra®	

Reporting group values	Nimenrix™ A Group	Nimenrix™ B Group	Menactra®MenACWY-DT 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

Reporting group values	Total		
Number of subjects	1011		
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)	0 0 0 0 0 0 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		

## End points

### End points reporting groups

Reporting group title	Nimenrix™ A Group
Reporting group description:	
Subjects received 1 dose of Nimenrix™ Lot A vaccine.	
Reporting group title	Nimenrix™ B Group
Reporting group description:	
Subjects received 1 dose of Nimenrix™ Lot B vaccine.	
Reporting group title	Menactra®MenACWY-DT Group
Reporting group description:	
Subjects were vaccinated with Menactra®	

### Primary: Number of subjects with vaccine response to hSBA-MenA, hSBA-MenC, hSBA-MenW-135, and hSBA-MenY antibodies

End point title	Number of subjects with vaccine response to hSBA-MenA, hSBA-MenC, hSBA-MenW-135, and hSBA-MenY antibodies <sup>[1][2]</sup>
End point description:	
End point type	Primary
End point timeframe:	
One month after the vaccination	

#### Notes:

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

Justification: The 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®Men ACWY-DT Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	310	297		
Units: Subjects				
hSBA-MenA	281	191		
hSBA-MenC	217	209		
hSBA-MenW-135	198	185		
hSBA-MenY	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 $\geq 1:4$



End point title	Number of subjects with hSBA-MenA, hSBA-MenC, hSBA-MenW-135, and hSBA-MenY antibody titers $\geq$ 1:4
End point description:	
End point type	Secondary
End point timeframe:	
One month after vaccination	

End point values	Nimenrix™ A Group	Nimenrix™ B Group	Menactra®Men ACWY-DT Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	315	309	305	
Units: Subjects				
hSBA-MenA (POST)	253	243	223	
hSBA-MenC (POST)	295	293	291	
hSBA-MenW-135 (POST)	272	262	247	
hSBA-MenY (POST)	307	302	287	

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with vaccine response to hSBA-MenA, hSBA-MenC, hSBA-MenW-135, and hSBA-MenY antibody titers $\geq$ 1:8

End point title	Number of subjects with vaccine response to hSBA-MenA, hSBA-MenC, hSBA-MenW-135, and hSBA-MenY antibody titers $\geq$ 1:8
End point description:	
End point type	Secondary
End point timeframe:	
One month after vaccination	

End point values	Nimenrix™ A Group	Nimenrix™ B Group	Menactra®Men ACWY-DT Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	315	309	305	
Units: Subjects				
hSBA-MenA (POST)	251	242	221	
hSBA-MenC (POST)	295	292	291	
hSBA-MenW-135 (POST)	272	262	247	
hSBA-MenY (POST)	307	302	287	

## Statistical analyses

No statistical analyses for this end point

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

End point title	Concentration of hSBA-MenA, hSBA-MenC, hSBA-MenW-135, and hSBA-MenY antibody titers
End point description:	
End point type	Secondary
End point timeframe:	
One month after vaccination	

End point values	Nimenrix™ A Group	Nimenrix™ B Group	Menactra®Men ACWY-DT Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	315	309	305	
Units: Titers				
geometric mean (confidence interval 95%)				
hSBA-MenA (POST)	54.2 (43.5 to 67.4)	49.6 (39.6 to 62.1)	41.3 (32.3 to 52.9)	
hSBA-MenC (POST)	687.1 (510.5 to 924.9)	755.8 (557.3 to 1025)	543.3 (411.2 to 718)	
hSBA-MenW-135 (POST)	174.5 (138.6 to 219.6)	161.6 (128.3 to 203.5)	101.7 (77.9 to 132.7)	
hSBA-MenY (POST)	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 MenACWY-TT-B	214			
hSBA-MenC MenACWY-TT-B	226			
hSBA-MenW- 135 MenACWY-TT-B	196			
hSBA-MenY MenACWY-TT-B	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:

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®Men ACWY-DT Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	329	329	325	
Units: Subjects				
Pain	169	167	180	
Redness	85	60	66	
Swelling	63	40	44	

### 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:

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®Men ACWY-DT Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	329	329	326	
Units: Subjects				
Fatigue	96	94	89	
Gastrointestinal	43	43	44	
Headache	86	87	83	
Temperature (Orally)	17	14	16	

### Statistical analyses

No statistical analyses for this end point

### Secondary: Occurrence of unsolicited non-serious adverse events

End point title	Occurrence of unsolicited non-serious adverse events
-----------------	--

End point description:

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®Men ACWY-DT Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	337	336	338	
Units: Subjects				
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)**

End point title	Number of subjects with occurrence of new onset of chronic illness(es) (NOCI)
End point description:	
End point type	Secondary
End point timeframe:	
From Month 0 through Month 6	

End point values	Nimenrix™ A Group	Nimenrix™ B Group	Menactra®Men ACWY-DT Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	337	336	338	
Units: Subjects				
NOCIs	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:	
End point type	Secondary
End point timeframe:	
From Month 0 through Month 6	

End point values	Nimenrix™ A Group	Nimenrix™ B Group	Menactra®Men ACWY-DT Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	337	336	338	
Units: Subjects				
All SAEs	0	0	0	

**Statistical analyses**

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Solicited symptoms during the 4-day post-vaccination period, Unsolicited AEs during the 31-day post-vaccination period, SAEs up to study end

Assessment type	Non-systematic
-----------------	----------------

### Dictionary used

Dictionary name	MedDRA
Dictionary version	10.0

### Reporting groups

Reporting group title	MenACWY-TT-A Group
Reporting group description: -	
Reporting group title	MenACWY-TT-B Group
Reporting group description: -	
Reporting group title	MenACWY-DT Group
Reporting group description: -	

Serious adverse events	MenACWY-TT-A Group	MenACWY-TT-B Group	MenACWY-DT 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 %

<b>Non-serious adverse events</b>	MenACWY-TT-A Group	MenACWY-TT-B Group	MenACWY-DT Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	169 / 337 (50.15%)	167 / 336 (49.70%)	180 / 338 (53.25%)
General disorders and administration site conditions			
Pain			
alternative assessment type: Systematic			
subjects affected / exposed	169 / 337 (50.15%)	167 / 336 (49.70%)	180 / 338 (53.25%)
occurrences (all)	169	167	180
Redness			
alternative assessment type: Systematic			

subjects affected / exposed	85 / 337 (25.22%)	60 / 336 (17.86%)	66 / 338 (19.53%)
occurrences (all)	85	60	66
Swelling			
alternative assessment type: Systematic			
subjects affected / exposed	63 / 337 (18.69%)	40 / 336 (11.90%)	44 / 338 (13.02%)
occurrences (all)	63	40	44
Fatigue			
alternative assessment type: Systematic			
subjects affected / exposed	96 / 337 (28.49%)	94 / 336 (27.98%)	89 / 338 (26.33%)
occurrences (all)	96	94	89
Gastrointestinal			
alternative assessment type: Systematic			
subjects affected / exposed	43 / 337 (12.76%)	43 / 336 (12.80%)	44 / 338 (13.02%)
occurrences (all)	43	43	44
Headache			
alternative assessment type: Systematic			
subjects affected / exposed	86 / 337 (25.52%)	87 / 336 (25.89%)	83 / 338 (24.56%)
occurrences (all)	86	87	83
Temperature (Orally)			
alternative assessment type: Systematic			
subjects affected / exposed	17 / 337 (5.04%)	14 / 336 (4.17%)	16 / 338 (4.73%)
occurrences (all)	17	14	16



## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 March 2010	<p>Amendment 3</p> <p>The introduction was updated with the current licensing status of competitor vaccines and the current recommendations for meningococcal vaccines.</p> <p>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.</p> <p>*Vaccine response is defined as an hSBA titer of at least 1:8 in subjects initially seronegative (hSBA titer &lt;1:4) and as a 4-fold increase in titer in subjects initially seropositive (hSBA titer 1:4).</p> <p>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:</p> <ul style="list-style-type: none"><li>• the World Health Organisation (WHO) considers SBA the primary means of assessing immune response to meningococcal conjugate vaccines [WHO, 2006;WHO, 1999]</li><li>• circulating bactericidal antibodies are more critical for persistent protection against meningococcal disease than non-functional antibodies against meningococcal polysaccharides [CDC, 2011; WHO, 2006].</li></ul> <p>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.</p>
06 September 2010	<ul style="list-style-type: none"><li>• The MenA capsular polysaccharide O-acetylation in MenACWY-TT vaccine Lot A will be 68% instead of 61%.</li><li>• Mencevax™ ACWY is not licensed in Canada.</li><li>• Menveo® (Novartis' meningococcal [groups A, C, Y and W-135] oligosaccharide diphtheria CRM197 conjugate vaccine) was recently licensed in Canada.</li><li>• A new abbreviation was added to the List of Abbreviations.</li><li>• For clarification, the word "days" was added after "180-210" in Table 3 Intervals between study visits.</li><li>• For clarification, the 31-day post-vaccination reporting period for pregnancies was added to Figure 1.</li><li>• New safety reporting telephone numbers replaced the old numbers.</li></ul> <p>New study contact for emergency code break telephone numbers replaced the old numbers.</p>

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported