Clinical trial results:
A phase III, open, randomized, controlled primary vaccination study to demonstrate the non-inferiority of meningococcal vaccine GSK134612 given intramuscularly versus Mencevax™ ACWY given subcutaneously to healthy subjects aged 2 through 10 years of age

Summary

EudraCT number	2012-000283-23
Trial protocol	Outside EU/EEA
Global end of trial date	06 January 2009

Results information

Result version number	v2
This version publication date	11 August 2016
First version publication date	25 April 2015
Version creation reason	• Correction of full data set Data (typos) were corrected .

Trial information

Trial identification

Sponsor protocol code	109495

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00514904
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)	Yes
EMA paediatric investigation plan number(s)	EMEA-000429-PIP01-08
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	20 May 2009
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 September 2008
Global end of trial reached?	Yes
Global end of trial date	06 January 2009
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Within 4 days after vaccination, in all subjects:
- To demonstrate the non-inferiority of meningococcal vaccine GSK134612 as compared to the licensed Mencevax ACWY in terms of the incidence of any grade 3 systemic symptoms.
One month after vaccination, in the immunogenicity subset corresponding to the first 1125 enrolled subjects:
- To demonstrate the non-inferiority of the vaccine response induced by meningococcal vaccine GSK134612 when compared to the licensed Mencevax ACWY in terms of serum bactericidal antibodies.

Protection of trial subjects:

All subjects were supervised for 30 min after vaccination administration with appropriate medical treatment readily available. Vaccines were administered by qualified and trained personnel only to eligible subjects that had no contraindications to any components of the vaccines. Subjects were followed-up from the day of vaccination and the subsequent 30 days after the last vaccination administration.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 September 2007
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	Saudi Arabia: 102
Country: Number of subjects enrolled	Lebanon: 201
Country: Number of subjects enrolled	Philippines: 800
Country: Number of subjects enrolled	India: 401
Worldwide total number of subjects	1504
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)	1504
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

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	1504
Number of subjects completed	1501

Pre-assignment subject non-completion reasons

Reason: Number of subjects	No vaccination: 3

Period 1

Period 1 title	Active+ESFU Phase (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Nimenrix™ Group

Arm description:

Subjects received 1 dose of Nimenrix™ vaccine at Month 0. Nimenrix™ vaccine was administered intramuscularly into the deltoid region of the non-dominant arm.

Arm type	Experimental
Investigational medicinal product name	Nimenrix™
Investigational medicinal product code	
Other name	MenACWY conjugate vaccine
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Single dose, intramuscular injection into the deltoid region of the non-dominant arm at Month 0.

Arm title	Mencevax ACWY Group

Arm description:

Subjects received 1 dose of Mencevax ACWY vaccine at Month 0. Mencevax ACWY vaccine was administered subcutaneously into the upper region of the non-dominant arm.

Arm type	Active comparator
Investigational medicinal product name	Mencevax ACWY
Investigational medicinal product code	MenACWY
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Single dose, subcutaneous injection into the upper region of the non-dominant arm.

Number of subjects in period 1[1]	Nimenrix™ Group	Mencevax ACWY Group
Started	1125	376
Completed	1101	371
Not completed	24	5
Consent withdrawn by subject	3	2
Lost to follow-up	21	3

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: Details provided in the Pre-assignment period.

Baseline characteristics

Reporting groups	
Reporting group title	Nimenrix™ Group
Reporting group description:	
Subjects received 1 dose of Nimenrix™ vaccine at Month 0. Nimenrix™ vaccine was administered intramuscularly into the deltoid region of the non-dominant arm.	
Reporting group title	Mencevax ACWY Group
Reporting group description:	
Subjects received 1 dose of Mencevax ACWY vaccine at Month 0. Mencevax ACWY vaccine was administered subcutaneously into the upper region of the non-dominant arm.	

Reporting group values	Nimenrix™ Group	Mencevax ACWY Group	Total
Number of subjects	1125	376	1501
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	5.6	5.5	
standard deviation	± 2.49	± 2.45	-
Gender categorical			
Units: Subjects			
Female	526	175	701
Male	599	201	800

End points

End points reporting groups

Reporting group title	Nimenrix™ Group
Reporting group description:	
Subjects received 1 dose of Nimenrix™ vaccine at Month 0. Nimenrix™ vaccine was administered intramuscularly into the deltoid region of the non-dominant arm.	
Reporting group title	Mencevax ACWY Group
Reporting group description:	
Subjects received 1 dose of Mencevax ACWY vaccine at Month 0. Mencevax ACWY vaccine was administered subcutaneously into the upper region of the non-dominant arm.	

Primary: Number of subjects with vaccine response to N. meningitidis serogroups A (MenA), MenC, MenY and MenW-135

End point title	Number of subjects with vaccine response to N. meningitidis serogroups A (MenA), MenC, MenY and MenW-135
End point description:	
Vaccine response was defined as an rSBA titer of at least 1:32 in subjects initially seronegative (< 1:8) and as 4-fold increase in titer from pre- to post-vaccination in subjects initially seropositive (≥ 1:8).	
End point type	Primary
End point timeframe:	
One month after vaccination (Post-vaccination, study Month 1)	

End point values	Nimenrix™ Group	Mencevax ACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	723	240		
Units: Subjects				
rSBA-MenA [N=594;192]	529	124		
rSBA-MenC [N=691;234]	664	210		
rSBA-MenW-135 [N=691;236]	673	195		
rSBA-MenY [N=723;240]	670	165		

Statistical analyses

Statistical analysis title	Difference vaccine response to anti-rSBA-MenW135
Statistical analysis description:	
To demonstrate the non-inferiority of the vaccine response induced by Nimenrix conjugate vaccine when compared to Mencevax ACWY vaccine for Neisseria meningitidis serogroup W-135 in terms of serum bactericidal antibodies using baby rabbit complement (rSBA).	
Comparison groups	Nimenrix™ Group v Mencevax ACWY Group

Number of subjects included in analysis	963
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Parameter estimate	Difference in percentage
Point estimate	14.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	10.26
upper limit	20.23

Notes:

[1] - Non-inferiority criterion: Lower limit [LL] of the 2-sided standardized asymptotic 95% confidence interval [CI] ≥-10%.

Statistical analysis title	Difference vaccine response to anti-rSBA-MenA

Statistical analysis description:

To demonstrate the non-inferiority of the vaccine response induced by Nimenrix conjugate vaccine when compared to Mencevax ACWY vaccine for Neisseria meningitidis serogroup A in terms of serum bactericidal antibodies using baby rabbit complement (rSBA).

Comparison groups	Nimenrix™ Group v Mencevax ACWY Group
Number of subjects included in analysis	963
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
Parameter estimate	Difference in percentage
Point estimate	24.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	17.52
upper limit	31.87

Notes:

[2] - Non-inferiority criterion: Lower limit [LL] of the 2-sided standardized asymptotic 95% confidence interval [CI] ≥-10%.

Statistical analysis title	Difference vaccine response to anti-rSBA-MenC

Statistical analysis description:

To demonstrate the non-inferiority of the vaccine response induced by Nimenrix conjugate vaccine when compared to Mencevax ACWY vaccine for Neisseria meningitidis serogroup C in terms of serum bactericidal antibodies using baby rabbit complement (rSBA).

Comparison groups	Nimenrix™ Group v Mencevax ACWY Group
Number of subjects included in analysis	963
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
Parameter estimate	Difference in percentage
Point estimate	6.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.68
upper limit	11.08

Notes:

[3] - Non-inferiority criterion: Lower limit [LL] of the 2-sided standardized asymptotic 95% confidence interval [CI] ≥-10%.

Statistical analysis title	Difference in vaccine response to anti-rSBA-MenY

Statistical analysis description:

To demonstrate the non-inferiority of the vaccine response induced by Nimenrix conjugate vaccine when compared to Mencevax ACWY vaccine for Neisseria meningitidis serogroup Y in terms of serum bactericidal antibodies using baby rabbit complement (rSBA).

Comparison groups	Nimenrix™ Group v Mencevax ACWY Group
Number of subjects included in analysis	963
Analysis specification	Pre-specified
Analysis type	non-inferiority[4]
Parameter estimate	Difference in percentage
Point estimate	23.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	18.02
upper limit	30.3

Notes:

[4] - Non-inferiority criterion: Lower limit [LL] of the 2-sided standardized asymptotic 95% confidence interval [CI] ≥-10%.

Primary: Number of subjects with grade 3 general symptoms (solicited and unsolicited)

End point title	Number of subjects with grade 3 general symptoms (solicited and unsolicited)

End point description:

Grade 3 symptom= symptom that prevented normal, everyday activities

End point type	Primary

End point timeframe:

During the 4-day (Days 0-3) post-vaccination period

End point values	Nimenrix™ Group	Mencevax ACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1125	376		
Units: Subjects				
Subjects	10	1		

Statistical analyses

Statistical analysis title	Relative Risk for Grade 3 symptoms

Statistical analysis description:

To demonstrate the non-inferiority of Nimenrix conjugate vaccine as compared to Mencevax ACWY vaccine in terms of the incidence of any grade 3 general (solicited and unsolicited) symptoms.

Comparison groups	Nimenrix™ Group v Mencevax ACWY Group

Number of subjects included in analysis	1501
Analysis specification	Pre-specified
Analysis type	non-inferiority[5]
P-value	= 0.2202
Method	Chi-squared
Parameter estimate	Risk ratio (RR)
Point estimate	3.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.56
upper limit	20.25

Notes:

[5] - Criterion for assessment: upper limit of the two-sided standardized asymptotic 95% confidence interval (CI) for the ratio between Nimenrix Group and Mencevax ACWY Group being lower than or equal to the pre-defined clinical limit ratio of 3.0 in the percentage of subjects with any grade 3 general symptoms.

Secondary: Number of subjects with rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and rSBA-MenY) titers greater than or equal to the cut-off values

End point title	Number of subjects with rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and rSBA-MenY) titers greater than or equal to the cut-off values

End point description:

The cut-off values for the rSBA titers were ≥ 1:8 and ≥ 1:128 respectively.

End point type	Secondary

End point timeframe:

Prior to and one month after vaccination (Pre vaccination, study Month 0 and post vaccination, study Month 1),

End point values	Nimenrix™ Group	Mencevax ACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	742	250		
Units: Subjects				
rSBA-MenA ≥ 1:8, M0 [N=599;194]	491	162		
rSBA-MenA≥ 1:8, M1 [N=739;247]	739	246		
rSBA-MenA ≥ 1:128, M0 [N=599;194]	476	155		
rSBA-MenA≥ 1:128, M1 [N=739;247]	739	246		
rSBA-MenC≥ 1:8, M0 [N=692;237]	224	77		
rSBA-MenC≥ 1:8, M1 [N=742;248]	738	241		
rSBA-MenC ≥ 1:128 M0 [N=692;237]	157	51		
rSBA-MenC ≥ 1:128 M1 [N=742;248]	736	234		
rSBA-MenW-135 ≥ 1:8, M0 [N=693;237]	455	152		
rSBA-MenW-135 ≥ 1:8, M1 [N=742;250]	742	245		
rSBA-MenW-135. ≥ 1:128 M0 [N=693;237]	389	133		
rSBA-MenW-135 ≥ 1:128 M1 [N=742;250]	742	245		
rSBA-MenY ≥ 1:8, M0 [N=725;241]	630	198		
rSBA-MenY ≥ 1:8, M1 [N=742;250]	742	248		

rSBA-MenY≥ 1:128 M0 [N=725;241]	590	188		
rSBA-MenY ≥ 1:128 M1 [N=742;250]	742	246		

Statistical analyses

No statistical analyses for this end point

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

End point title	rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and rSBA-MenY antibody titers

End point description:

Antibody titers were expressed as geometric mean titers (GMTs).

End point type	Secondary

End point timeframe:

Prior to and one month after vaccination (Pre vaccination, study Month 0 and post vaccination, study Month 1),

End point values	Nimenrix™ Group	Mencevax ACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	742	250		
Units: Titer				
geometric mean (confidence interval 95%)				
rSBA-MenA, M0 [N=599;194]	219.1 (186.5 to 257.4)	227.7 (172.9 to 299.9)		
rSBA-MenA, M1 [N=739;247]	6343.3 (5998.3 to 6708.1)	2283.2 (2022.6 to 2577.3)		
rSBA-MenC, M0 [N=692;237]	14.5 (12.5 to 16.7)	14.2 (11.1 to 18.1)		
rSBA-MenC, M1 [N=742;248]	4813.1 (4342.1 to 5335.3)	1317 (1042.9 to 1663.3)		
rSBA-MenW-135, M0 [N=693;237]	80.1 (67.4 to 95.3)	68.8 (51.3 to 92.3)		
rSBA-MenW-135, M1 [N=742;250]	11543.2 (10872.7 to 12255.1)	2157.8 (1815.2 to 2565.1)		
rSBA-MenY, M0 [N=725;241]	310 (268.8 to 357.3)	241.7 (185.3 to 315.3)		
rSBA-MenY, M1 [N=742;250]	10825.1 (10232.7 to 11451.7)	2613.1 (2236.9 to 3052.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-tetanus toxoid (anti-TT) concentrations greater than or equal to the cut-off values

End point title	Number of subjects with anti-tetanus toxoid (anti-TT) concentrations greater than or equal to the cut-off values

End point description:

The cut-off values for anti-TT concentrations were ≥ 0.1 IU/mL and ≥ 1.0 IU/mL respectively.

End point type	Secondary

End point timeframe:

Prior to and one month after vaccination (Pre vaccination, study Month 0 and post vaccination, study Month 1),

End point values	Nimenrix™ Group	Mencevax ACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	743	250		
Units: Subjects				
Anti-TT ≥ 0.1 IU/mL, M0 [N=743;250]	635	220		
Anti-TT ≥ 0.1 IU/mL, M1 [N=740;249]	733	218		
Anti-TT ≥ 1.0 IU/mL, M0 [N=743;250]	296	107		
Anti-TT ≥1.0 IU/mL, M1 [N=740;249]	720	107		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-tetanus toxoid (anti-TT) antibody concentrations

End point title	Anti-tetanus toxoid (anti-TT) antibody concentrations

End point description:

Antibody concentrations were expressed as geometric mean concentrations (GMCs)

End point type	Secondary

End point timeframe:

Prior to and one month after vaccination (Pre vaccination, study Month 0 and post vaccination, study Month 1),

End point values	Nimenrix™ Group	Mencevax ACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	743	250		
Units: Titer				
geometric mean (confidence interval 95%)				
Anti-TT, M0 [N=743;250]	0.65 (0.577 to 0.731)	0.744 (0.609 to 0.908)		

Anti-TT, M1 [N=740;249]	21.731 (19.821 to 23.825)	0.709 (0.581 to 0.866)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-polysaccharide (anti-PS) concentrations greater than or equal to the cut-off values

End point title	Number of subjects with anti-polysaccharide (anti-PS) concentrations greater than or equal to the cut-off values

End point description:

The cut-off values for anti-PS concentrations were ≥0.3 µg/mL and ≥2.0 µg/mL respectively FOR THE ant- PSA, anti-PSC, anti-PSW-135 and anti-PSY antibodies respectively. One half of the subjects (50%, randomized) of the ATP cohort for immunogenicity was tested for anti-PSA and anti-PSC and the other half for anti-PSW-135 and anti-PSY.

End point type	Secondary

End point timeframe:

Prior to and one month after vaccination (Pre vaccination, study Month 0 and post vaccination, study Month 1).

End point values	Nimenrix™ Group	Mencevax ACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	370	128		
Units: Subjects				
Anti-PSA ≥ 0.3 µg/mL, M0 [N=354;124]	154	41		
Anti-PSA ≥ 0.3 µg/mL, M1 [N=370;128]	369	126		
Anti-PSA ≥ 2.0 µg/mL, M0 [N=354;124]	59	12		
Anti-PSA ≥ 2.0 µg/mL, M1 [N=370;128]	368	123		
Anti-PSC ≥ 0.3 µg/mL, M0 [N=368;127]	29	7		
Anti-PSC ≥ 0.3 µg/mL, M1 [N=366;127]	365	127		
Anti-PSC ≥ 2.0 µg/mL, M0 [N=368;127]	12	2		
Anti-PSC ≥ 2.0 µg/mL M1 [N=366;127]	363	125		
Anti-PSW-135 ≥ 0.3 µg/mL, M0 [N=364;121]	18	11		
Anti-PSW-135 ≥ 0.3 µg/mL, M1 [N=370;121]	368	121		
Anti-PSW-135 ≥ 2.0 µg/mL M0 [N=364;121]	5	2		
Anti-PSW-135 ≥ 2.0 µg/mL M1 [N=370;121]	353	112		
Anti-PSY ≥ 0.3 µg/mL, M0 [N=368;121]	28	16		
Anti-PSY ≥ 0.3 µg/mL, M1 [N=370;122]	369	122		
Anti-PSY ≥ 2.0 µg/mL, M0 [N=368;121]	11	4		
Anti-PSY ≥ 2.0 µg/mL, M1 [N=370;122]	362	118		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-polysaccharide (anti-PS) antibody concentrations

End point title	Anti-polysaccharide (anti-PS) antibody concentrations

End point description:

Anti-PS concentrations were expressed as geometric mean concentrations (GMCs) and expressed in µg/mL One half of the subjects (50%, randomized) of the ATP cohort for immunogenicity was tested for anti-PSA and anti-PSC and the other half for anti-PSW-135 and anti-PSY.

End point type	Secondary

End point timeframe:

Prior to and one month after vaccination (Pre vaccination, study Month 0 and post vaccination, study Month 1).

End point values	Nimenrix™ Group	Mencevax ACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	370	128		
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-PSA, M0 [N=354,124]	0.4 (0.35 to 0.46)	0.29 (0.24 to 0.36)		
Anti-PSA, M1 [N=370,128]	81.1 (71.34 to 92.2)	25.43 (19.66 to 32.9)		
Anti-PSC, M0 [N=368,127]	0.18 (0.17 to 0.19)	0.17 (0.15 to 0.18)		
Anti-PSC, M1 [N=366,127]	22.61 (20.24 to 25.25)	25.69 (21.3 to 30.99)		
Anti-PSW-135, M0 [N=364,121]	0.17 (0.16 to 0.18)	0.17 (0.16 to 0.19)		
Anti-PSW-135, M1 [N=370,121]	12.8 (11.32 to 14.48)	13.85 (10.93 to 17.53)		
Anti-PSY, M0 [N=368,121]	0.18 (0.17 to 0.2)	0.2 (0.17 to 0.23)		
Anti-PSY, M1 [N=370,122]	19.26 (17.1 to 21.69)	22.71 (18.13 to 28.46)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects < 6 years of age with solicited local symptoms

End point title	Number of subjects < 6 years of age with solicited local symptoms

End point description:

Solicited local symptoms assessed were pain, redness and swelling.

End point type	Secondary

End point timeframe:

During the 4-day (Days 0-3) follow-up period after vaccination.

End point values	Nimenrix™ Group	Mencevax ACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	575	188		
Units: Subjects				
Any Pain	104	39		
Any Redness	82	31		
Any Swelling	31	15		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects ≥ 6 years of age with solicited local symptoms

End point title	Number of subjects ≥ 6 years of age with solicited local symptoms

End point description:

Solicited local symptoms assessed were pain, redness and swelling

End point type	Secondary

End point timeframe:

During the 4-day (Days 0-3) follow-up period after vaccination.

End point values	Nimenrix™ Group	Mencevax ACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	542	186		
Units: Subjects				
Any Pain	105	50		
Any Redness	107	36		
Any Swelling	54	16		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects < 6 years of age with solicited general symptoms	
End point title	Number of subjects < 6 years of age with solicited general symptoms

End point description:

Solicited general symptoms assessed were drowsiness, fever (measured orally and temperature ≥ 37.5°C), irritability and loss of appetite

End point type	Secondary

End point timeframe:

During the 4-day (Days 0-3) follow-up period after vaccination

End point values	Nimenrix™ Group	Mencevax ACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	575	188		
Units: Subjects				
Any Drowsiness	34	5		
Fever ≥ 37.5°C	50	12		
Any Irritability	31	6		
Any Loss of apptite	35	6		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects ≥ 6 years of age with solicited general symptoms	
End point title	Number of subjects ≥ 6 years of age with solicited general symptoms

End point description:

Solicited general symptoms assessed were fatigue, fever (measured orally and temperature ≥ 37.5°C), gastrointestinal and headache

End point type	Secondary

End point timeframe:

During the 4-day (Days 0-3) follow-up period after vaccination.

End point values	Nimenrix™ Group	Mencevax ACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	542	186		
Units: Subjects				
Any Fatigue	33	19		
Fever ≥ 37.5°C	48	19		
Any Gastrointestinal	25	15		
Any Headache	51	19		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting specific adverse events (AEs)

End point title	Number of subjects reporting specific adverse events (AEs)

End point description:

Specific AEs include:
– rash (hives, idiopathic thrombocytopenic purpura, petechiae),
– new onset of chronic illness(es) (NOCI) (e.g. autoimmune disorders, asthma, type I diabetes and allergies), and/or:
– conditions prompting emergency room (ER) visits or or non-routine physician office visits (i.e. office visits not related to well-being care, vaccination, injury or common acute illnesses such as upper respiratory tract infections, otitis media, pharyngitis, gastroenteritis)

End point type	Secondary

End point timeframe:

From Day 0 up to 6 months after vaccination

End point values	Nimenrix™ Group	Mencevax ACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1125	376		
Units: Subjects				
Rash (es)	45	16		
NOCI (s)	3	1		
ER visit (s)	15	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any unsolicited symptoms

End point title	Number of subjects reporting any unsolicited symptoms

End point description:

Unsolicited symptom covers any symptom 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:

Up to one month (Day 0-Day 30) after vaccination

End point values	Nimenrix™ Group	Mencevax ACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1125	376		
Units: Subjects				
Any (AE's)	198	75		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any serious adverse events (SAEs)

End point title	Number of subjects reporting any 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, 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 Day 0 up to 6 months after vaccination

End point values	Nimenrix™ Group	Mencevax ACWY Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1125	376		
Units: Subjects				
Any (SAE's)	15	7		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Serious adverse events: from Day 0 up to 6 months after vaccination. Solicited symptoms: during the 4-day (Day 0-Day 3) follow-up period after vaccination.

Adverse event reporting additional description:

This is specific for each SAE/AE that is entered.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	12.0

Reporting groups

Reporting group title	MenACWY Group

Reporting group description: -

Reporting group title	MenACWY-TT Group

Reporting group description: -

Serious adverse events	MenACWY Group	MenACWY-TT Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 376 (1.86%)	15 / 1125 (1.33%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	0 / 376 (0.00%)	1 / 1125 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Enteritis			
subjects affected / exposed	0 / 376 (0.00%)	1 / 1125 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperchlorhydria			
subjects affected / exposed	0 / 376 (0.00%)	1 / 1125 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			

Asthma			
subjects affected / exposed	1 / 376 (0.27%)	1 / 1125 (0.09%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhinitis allergic			
subjects affected / exposed	0 / 376 (0.00%)	1 / 1125 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 376 (0.00%)	1 / 1125 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	3 / 376 (0.80%)	3 / 1125 (0.27%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Typhoid fever			
subjects affected / exposed	2 / 376 (0.53%)	2 / 1125 (0.18%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 376 (0.27%)	3 / 1125 (0.27%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dengue fever			
subjects affected / exposed	0 / 376 (0.00%)	2 / 1125 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media			
subjects affected / exposed	0 / 376 (0.00%)	2 / 1125 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Viral infection			
subjects affected / exposed	0 / 376 (0.00%)	2 / 1125 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Amoebic dysentery			
subjects affected / exposed	0 / 376 (0.00%)	1 / 1125 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	1 / 376 (0.27%)	0 / 1125 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parasitic gastroenteritis			
subjects affected / exposed	0 / 376 (0.00%)	1 / 1125 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngotonsillitis			
subjects affected / exposed	1 / 376 (0.27%)	0 / 1125 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 376 (0.27%)	0 / 1125 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	0 / 376 (0.00%)	1 / 1125 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Food intolerance			
subjects affected / exposed	0 / 376 (0.00%)	1 / 1125 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	MenACWY Group	MenACWY-TT Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	50 / 376 (13.30%)	107 / 1125 (9.51%)	
General disorders and administration site conditions			
Pain (< 6 years of age)	Additional description: Assessed during the 4-day (Days 0-3) post-vaccination period in subjects < 6 years of age.		
alternative assessment type: Systematic			
subjects affected / exposed[1]	39 / 188 (20.74%)	104 / 575 (18.09%)	
occurrences (all)	39	104	
Redness (< 6 years of age)	Additional description: Assessed during the 4-day (Days 0-3) post-vaccination period in subjects < 6 years of age.		
alternative assessment type: Systematic			
subjects affected / exposed[2]	31 / 188 (16.49%)	82 / 575 (14.26%)	
occurrences (all)	31	82	
Swelling (< 6 years of age)	Additional description: Assessed during the 4-day (Days 0-3) post-vaccination period in subjects 2-5 years of age.		
alternative assessment type: Systematic			
subjects affected / exposed[3]	15 / 188 (7.98%)	31 / 575 (5.39%)	
occurrences (all)	15	31	
Pain (≥ 6 years of age)	Additional description: Additional description: Assessed during the 4-day (Days 0-3) post-vaccination period in subjects ≥ 6 years of age		
alternative assessment type: Systematic			
subjects affected / exposed[4]	50 / 186 (26.88%)	105 / 542 (19.37%)	
occurrences (all)	50	105	
Redness (≥ 6 years of age)	Additional description: Assessed during the 4-day (Days 0-3) post-vaccination period in subjects ≥ 6 years of age		
alternative assessment type: Systematic			
subjects affected / exposed[5]	36 / 186 (19.35%)	107 / 542 (19.74%)	
occurrences (all)	36	107	
Swelling (≥ 6 years of age)	Additional description: Assessed during the 4-day (Days 0-3) post-vaccination period in subjects ≥ 6 years of age.		
alternative assessment type: Systematic			
subjects affected / exposed[6]	16 / 186 (8.60%)	54 / 542 (9.96%)	
occurrences (all)	16	54	
Drowsiness	Additional description: Assessed during the 4-day (Days 0-3) post-vaccination period in subjects < 6 years of age		
alternative assessment type: Systematic			

subjects affected / exposed[7]	5 / 188 (2.66%)	34 / 575 (5.91%)	
occurrences (all)	5	34	
Fever (Orally) (< 6 years of age)	Additional description: Assessed during the 4-day (Days 0-3) post-vaccination period in subjects < 6 years of age		
alternative assessment type: Systematic			
subjects affected / exposed[8]	12 / 188 (6.38%)	50 / 575 (8.70%)	
occurrences (all)	12	50	
Irritability	Additional description: Assessed during the 4-day (Days 0-3) post-vaccination period in subjects < 6 years of age		
alternative assessment type: Systematic			
subjects affected / exposed[9]	6 / 188 (3.19%)	31 / 575 (5.39%)	
occurrences (all)	6	31	
Loss of appetite	Additional description: Assessed during the 4-day (Days 0-3) post-vaccination period in subjects < 6 years of age		
alternative assessment type: Systematic			
subjects affected / exposed[10]	6 / 188 (3.19%)	35 / 575 (6.09%)	
occurrences (all)	6	35	
Fatigue	Additional description: Assessed during the 4-day (Days 0-3) post-vaccination period in subjects ≥ 6 years of age		
alternative assessment type: Systematic			
subjects affected / exposed[11]	19 / 186 (10.22%)	33 / 542 (6.09%)	
occurrences (all)	19	33	
Fever (Orally) (≥ 6 years of age)	Additional description: Assessed during the 4-day (Days 0-3) post-vaccination period in subjects ≥ 6 years of age		
alternative assessment type: Systematic			
subjects affected / exposed[12]	19 / 186 (10.22%)	48 / 542 (8.86%)	
occurrences (all)	19	48	
Gastrointestinal	Additional description: Assessed during the 4-day (Days 0-3) post-vaccination period in subjects ≥ 6 years of age		
alternative assessment type: Systematic			
subjects affected / exposed[13]	15 / 186 (8.06%)	25 / 542 (4.61%)	
occurrences (all)	15	25	
Headache	Additional description: Assessed during the 4-day (Days 0-3) post-vaccination period in subjects ≥ 6 years of age		
alternative assessment type: Systematic			
subjects affected / exposed[14]	19 / 186 (10.22%)	51 / 542 (9.41%)	
occurrences (all)	19	51	

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.
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[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.
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[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.
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[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.
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[8] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheets completed.
[9] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheets completed.
[10] - 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.
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[11] - 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.
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[12] - 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.
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[14] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheets completed.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported